THE EFFECT OF NEURAL SUBSTRATES OF DUAL TOP-DOWN CONTROL NETWORKS ON MODULATING SET-MAINTENANCE AND RAPID-ADAPTIVE PERFORMANCE

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The Effect of Neural Substrates of Dual Top-Down Control Networks on Modulating Set-maintenance and Rapid-adaptive Performance

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CERTIFICATE OF ORIGINALITY

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Lam Lok Hang

ABSTRACT

Background

Top-down control function is important for handling goal-directed actions. Two distinct top-down brain networks, cingulo-opercular network (CON) and fronto-parietal network (FPN), were identified for set-maintenance and rapid-adaptive control respectively. Emerging evidence showed that these two networks may interact with each other for handling tasks with higher top-down control demand. This study adopted transcranial magnetic stimulation (TMS) method to activate transiently representative brain substrates in the CON and FPN to enable better understanding the differential effect of substrates of two networks to handle different demand levels of set-maintenance and rapid-adaptive control.

Objectives

This two-phase study aimed to examine, under higher and lower demands of set-maintenance control and rapid-adaptive control, how the TMS-induced activation at the distinct substrates of the CON and the FPN may influence differentially on (1) the subsequent task performance; (2) the neural processes during task-set implementation and information processing; (3) the changes of effective connectivity during task-set implementation and information processing.

Methods

Younger adults (Phase 1: *N* = 13; mean age = 26.5 ± 4.1; Phase 2: *N* = 18, mean age=25 ± 4.9) were recruited to participate in a single task with Flanker task, and a dual task with Flanker and 2-back task was performed before and after iTBS stimulations that were applied at three selected sites corresponding to the substrates of the CON (i.e., ai/fO, dACC/msFC and aPFC), two substrates of the FPN (i.e., dlPFC and dFC) (Phase 2 only) and a control site (i.e., vertex). Reaction time and electroencephalogram data were recorded during the cognitive tasks. To achieve the objectives, repeated measure ANOVA was used to analyse the 1) behavioural performance of the Flanker task; 2) the mean amplitude difference between target stimulation and control stimulation of two event-related components, namely the stimulus-preceding negativity (SPN; -200 – 0ms) and N1 (150 – 300ms) component. The SPN and N1 results help to determine the time windows for later analysis of oscillation frequency. Then the isolated coherence analysis (ICoh) was used to examine the effect of stimulated substrates on the changes of effective connectivity in term of the theta- and alpha-band oscillations, which were verified by the time-frequency analysis (TFA) method.

Results

A shorter reaction time was found after iTBS stimulation at aI/fO of the CON and dlPFC of FPN under higher demand of set-maintenance and rapid-adaptive. ICoh analyses showed, during task-set implementation, iTBS-stimulated aI/fO altered the connectivity in which dlPFC received more theta-band oscillation from aI/fO, aPFC and dFC for handling higher set-maintenance and rapid-adaptive demand. During information processing, iTBS-stimulated dlPFC increased the flow of theta-band oscillation from dACC/msFC to dlPFC to handle higher rapid-adaptive demand while aI/fO and dACC/msFC decreased the flow of alpha-band oscillation to handle higher set-maintenance demand.

Conclusion

The findings of this study shed light on the mechanism for flexible cooperation between the dual top-down networks. This was shown in the influential effect of aI/fO of the CON and dlPFC of FPN on set-maintenance control and rapid-adaptive control, respectively. Furthermore, the results suggested that the changes of connectivity of the two top-down networks appear to be specific to different demands of set-maintenance and rapid-adaptive control for task-set implementation and information processing performances. There are significant implications of these results for training strategies to enhance the top-down control functions.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER ONE

INTRODUCTION

Chapter One offers an overview of two studies of the current thesis on investigating the effect of distinct neural substrates of two top-down networks on the subsequent performance, handling various set-maintenance and rapid-adaptive demands during task-set implementation and information processing functions. This chapter includes a statement of purpose with objectives of Study One and Two, the background and justification of the study, the research hypotheses, and ends with the chapter organisation of this thesis.

1.1 Statement of Purpose

Two top-down control networks, cingulo-opercular network (CON) and fronto-parietal network (FPN), that are responsible for set-maintenance control and rapid-adaptive control, respectively, were identified (Dosenbach et al., 2006, 2007 & 2008). It was suggested that the connectivity between networks changed during the task-state, compared with the resting-state, in order to handle additional cognitive demands (Cole et al., 2003; Gordon et al., 2016, 2018; Ito et al., 2017; Nozawa et al., 2014; Pillay et al., 2016; Shine et al., 2016). The current study examined whether the activation of neural substrates (sometimes referred as “members of a network) within the CON and FPN influence the subsequent set-maintenance and rapid-adaptive performance, under various levels cognitive demands, through changing the neural processes of dual networks, in terms of event-related potentials (ERPs) and effective connectivity across dual network members. ERPs may provide good temporal information of neural activities with respect to specific event while effective connectivity may offer information about direction flow of signals between two brain substrates. A dual- and single-task paradigm with the Flanker task and the 2-back tasks has been used to manipulate the higher and lower demands of set-maintenance and rapid-adaptive top-down control. Applying transcranial magnetic stimulation (TMS) on different substrates of dual networks, the temporary facilitation effect of the targeted network substrates on subsequent task performance could be observed as a result of the dynamic changes in neural processes within and between networks. The ERPs and effective connectivity results were used to investigate the changes of neural processes during the task-set implementation and information processing period.

The objectives for the current study were to:

1. To examine the differential effects of the TMS-induced activation of the three selected substrates of the CON, aI/fO, dACC/msFC and aPFC, on the enhancement of information processing performance under higher and lower demands of set-maintenance control.

2. To examine the differential effects of the TMS-induced activation at the three substrates of the CON, aI/fO, dACC/msFC and aPFC, and two neural substrates of the FPN, i.e., dlPFC and dFC, on the enhancement on the reaction time of the

Flanker task, under the higher and lower demands of set-maintenance control, and higher and lower demands of rapid-adaptive control.

3. a) To examine the differential effects of the TMS-induced activation at the three substrates of the CON, aI/fO, dACC/msFC and aPFC, and two substrates of the FPN, dlPFC and dFC on the neural process during i) task-set implementation and ii) information processing, in terms of the ERP components, SPN and N1 component, respectively, under the higher and lower demands of set-maintenance control, and higher and lower demands of rapid-adaptive control.

3. b) To examine the differential effects of the TMS-induced activation at the three substrates of the CON, aI/fO, dACC/msFC and aPFC, and two substrates of the FPN, dlPFC and dFC on the changes of effective connectivity during i) task-set implementation and ii) information processing, in terms of signal direction of the alpha- and theta-band oscillations, under the higher and lower demands of set-maintenance control, and higher and lower demands of rapid-adaptive control.

1.2 Background and Justifications

Top-down control refers to the cognitive ability to manipulate relevant information to achieve a situational goal or task (Braver, 2012; Dosenbach et al., 2008). It has been suggested that proactive and reactive types of top-down control are needed in order to handle a wide range of tasks concurrently in an effective manner (Braver, 2012; Dosenbach et al., 2008). Recent studies identified two types of top-down control, i.e., set-maintenance control and rapid-adaptive control (Dosenbach et al., 2006, 2007 & 2008). Set-maintenance control pertains to implementing proactively and sustaining task-set information while rapid-adaptive control pertains to adjusting to the moment-to-moment control mechanisms of relevant information (Dosenbach et al., 2006, 2007 & 2008). The functions of these two types of top-down control could be illustrated by a daily example of key searching among different objects on a table. Before searching, a task-set, which is an idea or a rule of the goal, would be generated and sustained in the mind. While this task-set is being sustained, mental effort will scan the environment and selectively pay attention to the targeted key, but not other items that irrelevant to the task-set. In this example, set-maintenance control sustains the key searching task-set while rapid-adaptive control processes the key-related information from the table. Set-maintenance control and rapid-adaptive control have been shown to be associated with the activation of the cingulo-opercular network (CON) and fronto-parietal network (FPN) respectively (Dosenbach et al., 2006, 2007 & 2008). However, interaction has been identified between these two networks with changing set-maintenance demands (Chand & Dhamala, 2017; Cole et al., 2013 & 2021; Ito et al., 2017; Nozawa et al., 2014; Pillay et al., 2016; Shine et al., 2016).

The relationship between substrates within the same network, e.g., the CON and FPN, was found to be a highly stable within-network functional connectivity (Cole et al., 2013 & 2021; Dosenbach et al., 2007 & 2008), while the between-network functional connectivity may change across networks during task performance (Chand & Dhamala, 2017; Cole et al., 2013 & 2021; Ito et al., 2017; Nozawa et al., 2014; Shine et al., 2016). For example, Cole et al.'s studies (2013 & 2021) showed the changes of functional connectivity between the CON and FPN by comparing the task-state functional connectivity with the resting-state functional connectivity. Chand et al. (2017) showed the change when comparing functional connectivity with a difficult task and an easy task. It was suggested that the between-network connectivity between the CON and FPN may change in order to handle tasks with different cognitive demands. Besides, some network substrates, aI/fO and dlPFC, may be highly associated with the changes of connectivity between the network to influence the top-down control performance (Chand & Dhamala, 2017; Sheffield et al., 2016).

Most of the previous studies used functional magnetic resonance imaging (fMRI) data to demonstrate the correlational relationship between the activities of network substrates across the task. However, these studies did not provide temporal information about the direction of the neural signals when there are connectivity changes found between dual networks. First, the changes of network connectivity were not examined within specific cognitive processes.

Second, correlational data does not provide the causal effect of each network substrate on the later changes of connectivity.

Though ERP method may not have spatial resolution about the cortical activation, it has the advantage of providing more precise temporal resolution of neural information. For example, when manipulation different set-maintenance demands by adopting the dual-task paradigm, it was shown that neural processes during task-set implementation (Karayanidis et al., 2011; Steinhauser & Steinhauser, 2018) and information processing (Gherri & Eimer, 2010; Little & Woollacott, 2015; Singhal et al., 2002) were affected. There are two ERP components found to be associated with set-maintenance and rapid-adaptive functions which are related to the CON and FPN. For example, Steinhauser and Steinhauser (2018) manipulated the demand of set-maintenance control by the sequence of the dual task. The results showed that the subsequently presented task, that had higher demand to implement task-set, elicited a more negative stimulus-preceding negativity (SPN) component during the pre-stimulus period. Another negative ERP component, called N1, is related to information processing. Gherri and Eimer (2010) demonstrated that, under a dual-task situation, information processing was influenced by a higher demand of the task-set compared with single-task situation and this neural process was reflected by less negative-going N1 component. It is suggested that, by manipulating different levels of set-maintenance demands, task-set implementation and information processing may be affected. While it was suggested that the functional connectivity between CON and FPN may be changed in order to handle higher set-maintenance demands, it is yet to be understood how the functional connectivity would be altered during task-set implementation and information processing period. Besides, a dual-task paradigm was used to manipulate cognitive demands and demonstrated the changes of neural processes in ERPs (Gherri & Eimer, 2010; Little & Woollacott, 2015; Singhal et al., 2002; Steinhauser & Steinhauser, 2018) and changes of the neural substrate activations in fMRI studies (Pillay et al., 2016). This study used a dual-task design to increase set-maintenance demands to trigger the changes of connectivity between the CON and FPN, in order to understand the underlying mechanism of dual networks in handling higher set-maintenance demands.

The current study used intermittent theta-burst transcranial magnetic stimulation (iTBS) as the TMS protocol to facilitate the specific brain substrates of dual top-down networks. The iTBS protocol was reviewed and shown facilitation effect in motor- (Chung et al., 2016) and cognitive-related (Lowe et al., 2018) brain substrates. The targeted substrate could influence the neural processes in order to enhance task performance, therefore, the facilitation of the iTBS stimulation at this substrate would further strengthen the changes of neural processes and, hence, the enhancement of task performance. In doing so, the causal effect of each dual-network substrates on the changes of neural processes and subsequent performance could be understood.

Furthermore, the isolated coherence (ICoh) analysis method was used to demonstrate the effective connectivity between dual network substrates. This is a multivariate autoregressive model, proposed by Pascual-Marqui et al. (2014), that can transform oscillation data to compute directionality connections between brain substrates. It was speculated that increased connectivity would be found between the CON and FPN with the theta-band oscillation during task-set implementation, and with the alpha-band oscillation during information processing.

1.3 Hypotheses

For each of the objectives listed in the previous section (p. 2-3), the hypotheses are described as follows:

For Objective One, it was hypothesised that the reaction time of information processing performance would be significantly decreased after the iTBS stimulation was applied at aI/fO, but not at dACC/msFC and aPFC, under the dual-task condition.

For Objective Two of Study Two, it was hypothesised that shorter reaction time of the Flanker task would be found after stimulating at aI/fO and dlPFC, but not at dACC/msFC, aPFC and dFC, under the incongruent trials of the dual-task condition.

For Objective 3a of Study Two, it was hypothesised that i) iTBS stimulation at aI/fO of the CON may facilitate the task-set implementation, as indicated by a more negative-going SPN component in the dual-task condition compared with the single-task condition compared to other CON substrates, i.e., dACC/msFC and aPFC, and FPN substrates, dlPFC and dFC; ii) iTBS stimulation at dlPFC of the FPN would facilitate the information processing as indicated by a less negative-going N1 component under the incongruent trials of the dual-task condition compared to the CON substrates, i.e., aI/fO, dACC/msFC and aPFC, and the FPN substrates, dFC.

For Objective 3b of Study Two, it was hypothesised that i) stimulation at aI/fO of the CON may lead to bidirectional flows of the theta-band oscillation found between aI/fO and dlPFC when handling a higher demanding situation. Also, it was hypothesised that the flows of the theta-band oscillation sent from aI/fO to the FPN substrates and also from dFC to the CON substrates. For the information processing period, it was hypothesised that ii) stimulation at dlPFC of the FPN may increase the effective connectivity of the alpha-band oscillation under the higher demand of set-maintenance and rapid-adaptive. First, the aI/fO and dlPFC may have bidirectional flows of the alpha-band oscillation found. Also, there should be increased information flows of the alpha-band sent from aI/fO to the other substrates within the CON and sent from dlPFC to the other substrates within FPN substrates.

1.4 Study Significance

The current study sheds light on the underlying processes of two top-down control networks, the CON and FPN, during task-set implementation and information processing under various cognitive demands. First, it may give extra evidence in the causal effect of each dual network substrate on the subsequent changes of neural processes and task performance. Second, the current study may also provide new information for the differential changes of two networks with various cognitive demands. Third, it also may provide new information about the connectivity changes of two networks during specific cognitive processes, i.e., task-set implementation and information processing. Altogether, it may give insights on the training approaches to ameliorate the functions related to the top-down control processes of individuals who requires functional enhancement (e.g., those with cognitive decline).

1.5 Organisation of the Chapters

This thesis consists of six chapters. Other than this chapter (Chapter One) gives the overview of the study, Chapter Two reviews literatures of top-down control with corresponding top-down networks, ERP and TMS studies on top-down control. Chapter Three describes the methodology and analysis method of Study One, TMS-behavioural study, and Study Two, TMS-EEG study. Chapter Four reports the results including behavioural results of Study One and Study Two, and the results of the ERPs and effective connectivity, which used ICoh. Chapter Five covers the discussion of the three types of results reported. The final chapter includes the main findings, limitations, and future investigations.

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CHAPTER TWO

LITERATURE REVIEW

2.1 Dual Networks of Top-down Control

Top-down control describes the cognitive ability to achieve a situational goal through the processing of relevant upcoming information based on preset task rules or task-sets (Braver, 2012; Dosenbach et al., 2008). Recently, it was suggested that the top-down control function can be manipulated by proactive and reactive types of top-down control (Braver, 2012; Dosenbach et al., 2008). Proactive type of top-down control refers to the implementation and maintenance of the task-set that this process may enhance the preparation of the task-set and reduce the interference of distraction (Braver, 2012; Dosenbach et al., 2008). However, it may limit the availability of information that is not directly related to the task and this information may be regarded as a distraction. On the other hand, reactive type of top-down control refers to the moment-to-moment activation of a task-set based on a certain triggered event (Braver, 2012; Dosenbach et al., 2008). It may provide flexibility to the process task-set effectively based on the triggering that tends to be relatively short term. Compared with proactive types of top-down control, it may need a salient event to trigger the processing of the task-set that would be less stable across time.

A series of functional magnetic resonance imaging (fMRI) and resting-state MRI (rsMRI) studies identified two brain networks, namely the cingulo-opercular network (CON) and fronto-parietal network (FPN) that were responsible for set-maintenance top-down control and rapid-adaptive top-down control, which were in a more proactive and reactive manner respectively (Dosenbach et al., 2006, 2007 & 2008). To explore different brain regions related to set-maintenance and rapid-adaptive control, Dosenbach and colleagues (2006, 2007 & 2008) explored the co-activated regions of the brain with ten different types of tasks including searching, identification, and judgment. They marked events of start-cue and each trial across all blocks of the ten tasks. Hence, the brain substrates could be classified with different functionalities based on their activation pattern corresponding to different types of events. Besides, to understand how the brain substrates were related to task performance, the differences between the brain activation during correct and error trials were computed as error-related activity. As set-maintenance control functions to implement and maintain task-set information proactively and continuously, the corresponding brain substrates were found to be activated across the different tasks. The brain substrates of the set-maintenance control network, the CON, were found to have a sustained activation pattern across the start-cue and each trial as well as the error-related activity. The results revealed that anterior insula/frontal operculum (aI/fO), dorsal anterior cingulate cortex/medial superior frontal cortex (dACC/msFC), and anterior prefrontal cortex (aPFC) subserved the set-maintenance control function. Though all three network substrates, aI/fO, dACC/msFC and aPFC showed activation across the different processes of a task, it was found that aPFC activated across only smaller amounts of the ten tasks compared with aI/fO and dACC/msFC. This implied more specific criteria were required to elicit the activation of aPFC while the activation of aI/fO, dACC/msFC would be relatively general to implement and sustain different types of task-set information. It has been suggested that the activation of aPFC is responsible for high-demands of task-set situations, for example, dual-task (Pillay et al., 2016), task-switch paradigm (Braver et al., 2003), or paradigm with prolonged pre-stimulus interval (Sakai & Passingham, 2003). The rapid-adaptive control, it may manage moment-to-moment control based on the triggering event (Dosenbach et al., 2006, 2007 & 2008). It has been suggested that the corresponding brain substrates were activated during the initiation of a trials or processing trials-based task relevant information. The results showed the intraparietal sulcus (IPS) and dorsal frontal cortex (dFC) subserved the trials initiation while the dorsolateral prefrontal cortex (dlPFC) subserved the processing of the relevant information of a trial. When using independent component analysis, it was further suggested that dlPFC, IPS and dFC may work together as the rapid-adaptive control network, i.e., the FPN (Dosenbach et al., 2007). While it was shown that the substrates of the CON and FPN may work tightly for set-maintenance and rapid-adaptive top-down control. It seemed that each of the network substrates may have differential effects on the various situations. This will be discussed in the following section.

2.2 The Differential Activation Pattern across Substrates of the Dual Networks during High Demand of Set-maintenance Control

While the substrates of the CON and FPN were shown to work tightly within their own network, there were different activation patterns found for certain task situations. It was speculated that this altered pattern may relate to the more influential role of a network substrate to a specific process. The dual-task paradigm was one of the experimental designs that may elicit differential activation of substrates within each of the dual networks (Kondo et al., 2004; Pillay et al., 2016). Pillay et al. (2016) used an additional task-set, that required the sustained inhibition of distraction on top of the auditory detection task, to contrast the higher and lower demands of set-maintenance. Under the higher demand of set-maintenance control, stronger activation was found in the substrates of the CON, including aI/fO, dACC/msFC and aPFC, and the substrates of the FPN, dlPFC. There were two observations. First, consistent with the studies of Dosenbach and colleagues (2006 & 2007), the substrates of the CON were shown to be responsible for sustained task-set information and stronger activation of the aI/fO, dACC/msFC and aPFC which may be required to help in handling extra task-set information. Second, some of the FPN substrates, i.e., dlPFC, may be flexibly involved to handle extra task-set demand, but not only engaged in the processing of task relevant information. This was further supported in a study conducted by Kondo et al. (2004), in which a dual-task paradigm was also adopted to examine how the activation of brain substrates were different between good and poor performers. The participants in the study were required to judge whether a letter presented was a normal or mirror image, and simultaneously remember the directions of the arrows. While the direction of the arrows was needed to be remembered across the block of tasks, the participants were needed to implement the task-set of the judgement task at the same time. Under this situation with such a high demand of set-maintenance, the results revealed the association between the msFC/dACC and dlPFC were found in only those with good performance but not those with poor performance. It supported the notion that dlPFC, the substrate of the FPN, would be involved to enhance subsequent performance with handling the extra demand of set-maintenance control. Besides, this enhancement of performance may be related to the association between msFC/dACC and dlPFC. It was speculated that, not only the co-activation of substrates of the networks, but interaction between substrates may be important to facilitate the top-down control which was demanded by extra task-sets. A number of task-state fMRI studies, hence, have investigated how the demand of set-maintenance control may be related to the changes of the connectivity between networks.

2.3 Changes of Functional Connectivity between Dual Networks under High Set-maintenance Demand

Functional connectivity, which is a statistical method to show the relationship between two brain substrates, was found to be high and stable among the brain substrates within the CON and FPN (Dosenbach et al., 2006, 2007 & 2008; Gordon et al., 2017; Power et al., 2011) while their between-network connectivity was found to have changed during task-state compared with a resting state (Cole et al., 2021; Gordon et al., 2016; Nozawa et al., 2014; Pillay et al., 2016). This implied that when there is any task-sets existing, the changes of between-network connectivity would need to be altered and sustained in order to handle multiple tasksets. Cole et al. (2013) investigated how different brain networks may change generally under task-state to contrast with the resting-state. They manipulated the task-sets by combining the rules across three distinct domains, namely, logical decision, sensory semantic, and motor response in the task. The variation of functional connectivity between each substrate of whole brain networks across all of the connections were measured and the variability of between-network functionality across a total of 64 types of task-sets was computed. The results showed that the changes of functional connectivity between the CON and FPN was higher than average. This indicated that the changes of functional connectivity between the CON and FPN was essential to accomplish different types of task-sets. Cole et al. (2021) further used the task-state and resting-state functional connectivity across whole brain networks to predict the brain activation pattern, which represented the subsequent behavioural performance, among 24 different task-sets. The study revealed more accurate results using the task-state network functional connectivity compared with the resting-state one. This implied that the changes of between-network functional connectivity were related to the effectiveness of handling various task-sets. However, Cole et al.'s studies (2013 & 2021) did not show how the functional connectivity changed across the substrates within the CON and FPN. Other studies demonstrated how different substrates may relate with functional connectivity change (Chand & Dhamala, 2017; Sheffield et al., 2016). Sheffield et al. (2016) examined the relationship between the between network functionality of the CON and FPN substrates. They measured the performance of different tasks including memory, processing speed, goal maintenance, and visual integration and computed an overall cognitive score. This score was then used to examine the correlation with the task-state functional connectivity of each substrate of the CON and FPN. The results revealed only a significant relationship between aI/fO, the substrate of the CON, with the overall cognitive performance. It seemed that the aI/fO may have a major role to functionally connect with other network substrates to process corresponding task-sets. Interestingly, Chand and Dhamala (2017) found inconsistent results of Sheffield et al. (2016) with a different analysis method. A face-house perceptual categorisation task was used with the electroencephalography (EEG) recorded. The EEG oscillation information of the correct trials was then extracted during both the attention period and the decision-making period. The information outflow from the substrates of the CON and FPN to other substrates was then calculated by spectral Granger causality analysis. The results revealed that increased flow of oscillations was sent from aI/fO and dACC/msFC to dlPFC during the attention period, while increase flow of oscillation was sent from dlPFC to aI/fO and dACC/msFC during the decision-making period. Unlike the study of Sheffield et al. (2016) which showed the possible dominant role of specific substrates, Chand and Dhamala (2017) demonstrated that the influential effect of different substrates on functional connectivity could be changed across different processes of a task. Hence, a specific cognitive process would be one of the important factors to understand the changes of the between network connectivity when related to the set-maintenance and rapid-adaptive top-down control.

2.4 Timing of Top-down Control in Dual Networks

Previous fMRI studies provided information about the relationship between dual network substrates based on the changes of the blood-oxygen-level-dependent (BOLD) signals. There was a time delay during measurement and lack of information about the temporal details on the changes of the CON and FPN on handling set-maintenance and rapid-adaptive control during different periods of task. ERP studies provided good temporal information about top-down control processes, including the task-set implementation of set-maintenance control (Brunia et al., 2012; Kang et al., 2014; van Boxtel & Böcker, 2004; Steinhauser & Steinhauser, 2018) and information processing of rapid-adaptive control (Bueno et al., 2013; Gherri & Eimer, 2010; Hillyard & Anllo-Vento, 1998). The task-set implementation and information processing were also investigated when manipulating the demand of set-maintenance control in the dual-task paradigm. This will be further discussed in the following section.

The key function of the CON is related to task-set implementation while the FPN is related to the moment-to-moment information processing (Dosenbach et al., 2006, 2007 & 2008). The CON showed activation during the start-cue and also sustained activation across each trial of the ten different tasks in the study conducted by Dosenbach et al. (2006). Though the CON may sustain the task-set stably across time, one of its main functions is to implement the upcoming task-set (Dosenbach et al., 2006, 2007 & 2008). It was revealed that the CON, compared with the FPN, would be much more engaged during the implementation period of a task. An EEG-fMRI study conducted by Kotani et al. (2017) explored the corresponding brain substrates that were activated for the implemented task-set. The result revealed activation at the right aI/fO, the substrates of the CON, during the pre-stimulus period of time, indicated by the SPN component. Steinhauser and Steinhauser (2018) used a dual-task paradigm to influence the implementation of the task-set. The participants in their study were required to do both a Flanker task and a pitch discrimination task while the order was arranged in two different ways, either a Flanker task presented earlier or presented later. Hence, the rapid-adaptive demand was controlled in both conditions when the same Flanker task was done. The difference was the duration of the task-set implementation period in the two conditions. There was a longer implementation period for the condition when the Flanker task was presented first. For the condition with the Flanker task presented later, the participants needed to implement the task-set immediately after the discrimination task. The demand of the set-maintenance control would be relatively large to implement the task-set with a shorter period of time. It was found that the neural process during the pre-stimulus period was affected and reflected by a more negative-going SPN component, which has been found around 200ms before the onset of the stimulus (Brunia et al., 2012; van Boxtel and Böcker, 2004; Steinhauser & Steinhauser, 2018; van Boxtel & Böcker, 2004). Besides, Min and Park (2010) used another method to demonstrate the implementation of the upcoming task-set. They used a shape discrimination task with a long inter-stimulus interval. The participants were required to response to decide whether the shape of two presented stimuli were the same or not. During the long preparation time, the task-set was implemented and maintained to prepare for the up coming discrimination task. With using time-frequency analysis (TFA) method, the stronger theta-band oscillation was found in frontal regions of the brain during pre-stimulus period (i.e., from 300 to 50ms before stimulus onset). This result matched with the SPN component in ERP studies that showed the changes of brain activities in frontal regions during the period of task-set implementation.

The key role of the FPN is to process the moment-to-moment task relevant information (Dosenbach et al., 2006, 2007 & 2008). A stronger activation of the FPN was found for the initiation of a trials or the correctness of a trials. Therefore, the FPN should be more engaged once the target stimulus is presented from the environment and to react immediately with the target stimulus based on the task-set. The N1 component was one of the neural processes that was elicited by the perception of the target stimulus and varied by the changes of the pre-set rules (Doallo et al., 2005; Zhang et al., 2013). Furthermore, previous dual-task studies found the demand of the set-maintenance in a dual-task condition may influence not only the task-set implementation of the set-maintenance control, but also the information processing of the rapid-adaptive control. Gherri and Eimer (2010) used a single- and dual-task design study to contrast the neural processes demanded with the extra task-set. The participants needed to do a visual detection task whilst listening to an auditory recording. The listening task-set needed to be sustained across the information processing of the visual detection task. With a higher demand of set-maintenance during the information processing period, the N1 component became less negative going under the dual-task condition compared with the single-task condition (Gherri & Eimer, 2010; Little & Woollacott, 2015; Singhal et al., 2002). Similarly, Wang et al. (2018) also used single- and dual-task paradigm to show the effect of additional task-set on information processing. For the single-task condition, the participants were needed to either do a car driving task to direct the car back to the cruising lane, or a mental calculation task to decide whether an arithmetic equation was correct or not. For the dual-task condition, the participants were required to both driving task and mental calculation concurrently. The TFA results showed that the alpha-band oscillation in parietal area was decreased during information processing period (i.e., 0-500ms after the stimulus onset) in the dual-task condition compared with the single-task condition. It was suggested that the lowered alpha-band oscillation may due to the additional demand of information processing and reflected in longer reaction time used in dual-task condition. This result may also provide another evidence to support the N1 component in ERP studies may relate to the changes of brain activities for additional demand of information processing.

Both ERP components and oscillation frequency bands extracted in TFA method provided a specific time frame to understand how the demand of set-maintenance may influence the task-set implementation and information processing. However, there is a lack of evidence to show how the changes of functional connectivity between the CON and FPN may relate to these two neural processes. The changes of functional connectivity between the CON and FPN could be further investigated at the task-set implementation and information processing period, indicated by the SPN and N1 component. The SPN component has been found around 200ms immediately prior to the onset of the stimulus (Brunia et al., 2012; van Boxtel and Böcker, 2004; Steinhauser & Steinhauser, 2018; van Boxtel & Böcker, 2004). Its distribution happens to be at the frontocentral electrode sites. More negative-going SPN amplitude was found with higher cognitive demands when preparing an upcoming task-set, such as a dual-task condition (Steinhauser & Steinhauser, 2018). The N1 component is a negative component found around 150ms after the onset of a target stimulus (Fort et al., 2013; Gherri & Eimer, 2010; Hillyard & Anllo-Vento, 1998; Little & Woollacott, 2015; Singhal et al., 2002; Theeuwes, 2010). It may be distributed mainly in the parietal and occipital areas (Bueno et al., 2013; Gherri & Eimer, 2010; Little & Woollacott, 2015) while others reported in the frontal areas (Hillyard & Anllo-Vento, 1998; Singhal et al., 2002). The N1 component was showed less negative-going with higher cognitive demands when processing multiple task-set, such as a dual-task condition (Gherri & Eimer, 2010; Little & Woollacott, 2015; Singhal et al., 2002). The current study used a single-task and dual-task design to increase the demand of the set-maintenance control. It was speculated that the task-set implementation and information processing would be demanded by the extra task-set. The changes of functional connectivity between the CON and FPN should be found across these two processes in order to handle the higher demand of set-maintenance control.

2.5 TMS studies on Top-down Control in Dual Networks

To show the causal effect of the activations of the substrates of the FPN and CON on set-maintenance and rapid-adaptive control, transcranial magnetic stimulation (TMS) is one of the common stimulation methods used. The time course of FPN activation has been previously studied with the TMS method (e.g., Kehrer et al., 2015; Soutschek et al., 2016). In Kehrer et al.'s study (2015), their participants were instructed to indicate the location of the target circle from one out of four boxes. During the task, they were stimulated on either of the FPN substrates, right IPS or right dlPFC, at one of five time-points (i.e., 50, 100, 150, 200 and 250ms) after the target was presented. The reaction time was found to be faster when the TMS stimulations were applied at both the IPS and dlPFC when compared with the control stimulation at only 100ms after the stimulus target onset. It was shown that the TMS stimulation at both substrates of the FPN may facilitate the immediate processing of the external stimulus based on the preset task-set. These similar results after the stimulation at the two different substrates of the FPN were consistent with the highly co-activation pattern within the FPN showed in previous fMRI studies (Dosenbach et al., 2006, 2007 & 2008). Besides, this study showed that the facilitation of the FPN happened after the stimulation at a specific time window, 100ms. This implied that the predominant processing period of the FPN was short once the triggering event had happened. It matched with the characteristic of the FPN as previously discussed. However, it may not demonstrate the changes of connectivity across network substrates for the facilitation of performance after stimulation. Also, the single task design of the study may have relatively low demand of the set-maintenance control. It is yet to be understood how the stimulation of network substrates may be different under dual-task situations.

Another study, using a dual-task paradigm, explored the stimulation effect at the dACC/msFC, which is a substrate of the CON (Soutschek et al., 2016). In the dual-task paradigm, an auditory detection task was required to be completed which followed a visual detection task. With a TMS stimulation 100ms after the visual task onset, the study aimed to inhibit the processes of a finished auditory task-set and facilitate the upcoming visual task-set. Interestingly, the result showed that the stimulation facilitated not only the reaction time of the later visual task, but also the reaction time of the earlier auditory task. The stimulation appeared to facilitate the overall handling of the task-set for both the current trials and the next trials. It was suggested that the facilitation effect of the CON on set-maintenance control function, may implement and maintain multiple task-set effectively. Besides, the influence of both the current trials and the next trials showed the sustainable nature of the CON. The stimulation of the CON affected not only the short period of time after the stimulus but also the next trials which was over 1000ms. Different with the FPN, the CON may modulate the top-down control on a wider range of time period. This study provided extra evidence to support the function of the CON in the implementation of the task-set. However, only one substrate was stimulated in the study. The different stimulation effect on other CON substrates may not be compared. The previous studies showed different activation patterns among the three substrates of the CON, i.e., aI/fO, dACC/msFC and aPFC. The aI/fO seemed to be more associated with the subsequent performance in the study conducted by Sheffield et al. (2016). However, it is yet to be examined whether the activation of aI/fO with TMS may have more influence on the performance during higher set-maintenance demand compared with the other two substrates, dACC/msFC and aPFC.

Apart from behavioural studies, other resting-state MRI studies adopted TMS methodology to examine the connectivity between the CON and FPN (Gratton et al., 2013, 2014). A theta-burst stimulation (TBS) protocol was used to stimulate at either the aI/fO or the dlPFC in order to explore how they may influence within- and between- network connectivity. Compared with the control stimulation, the results showed increases both within- and between-network connectivity of both networks. It was shown that, when stimulating at aI/fO and dlPFC, the stronger activation was not only found at the stimulated substrates, but co-activation at the other substrates within and between their networks was also found. This demonstrated the influential effect of aI/fO and dlPFC on the connectivity between substrates of dual networks. These results were also consistent with the previous finding that showed high association between the activation of the aI/fO and dlPFC with between-network connectivity (Chand & Dhamala, 2017; Sheffield et al., 2016). The previous fMRI studies showed there were differences between the functional connectivity of the resting-state and task-state. While changes of connectivity between substrates of the dual networks may be required to handle extra task-set, the stimulation may strengthen the adjusted connectivity to facilitate the corresponding processes.

2.6 The Need of Directional Information for Understanding Specific Top-down Control Process

As discussed in Section 2.4 and 2.5 in which the evidence supported by previous ERP and TMS studies were discussed, the CON and FPN may have influence on different top-down control processes across a task, such as task-set implementation and information processing. However, it is yet understand how the dual-network substrates may influence the corresponding process. In order to understand the underlying mechanisms of the cooperation between dual networks, not only the connection between each dual-network substrate, but also the casual directionality between substrates could provide essential information to estimate the underlying processes. However, the directional information was addressed in few previous functional connectivity studies that involved measures with temporal information to provide directional estimation. For example, in Chand and Dhamala's study (2017), EEG method was used to show different direction of oscillatory signals measured between the CON and FPN during different time periods of a task. In a perceptual decision-making task, they extracted oscillatory activities of two defined time windows, from 25 to 225ms, and from 225 to 425ms of the target onset. With computed by Granger causal analysis, the results revealed the direction flows of oscillation signals were different in these two periods of time. The earlier time period showed more oscillatory signals sent from the CON to other network substrates while the subsequent time period showed more oscillatory signals sent from the FPN to other network substrates. It indicated the changes of connectivity may be dynamic across time. The directionality information would be important to understand underlying mechanism of specific processes, i.e., task-set implementation and information processing.

The ICoh analysis was used in the current thesis to investigate the directional functional connectivity with EEG oscillation data. This analysis was a type of multivariate autoregressive model that offers effective connectivity information, which is the causal influence of one region to another (Pascual-Marqui et al., 2014). Different from other autoregressive models, it is intended to remove all "indirect" connection paths by setting all irrelevant connections to zero.

Using oscillation data recording from the scalp, the electric neuronal activity from the location of each targeted substrate would be computed with inverse solution, exact low-resolution electromagnetic tomography (eLORETA; Pascual-Marqui, 2007, 2009; Pascual-Marqui et al., 2011). Hence, the inversed data could be further computed by ICoh for the direct pathways between each preset location. This analysis method has been applied in EEG studies in the resting state (Guerrero & Achermann, 2018) or task-state (Kitaura et al., 2017; Steinmann et al., 2018). Kitaura et al. (2017) examined how the connectivity between the substrates of dorsal and ventral attention networks may change under a calculation task, compared to resting state when using ICoh analysis. The result showed decreased flows of alpha- (8-12Hz) and theta-band (4-8Hz) oscillations from inferior frontal gyrus to anterior cingulate cortex, and increased flows of the alpha-band oscillation bidirectionally between superior temporal gyrus and inferior frontal gyrus. When using ICoh, beyond the changes of functional connectivity between network substrates, the results provide additional information for the direction flows of oscillations between selected substrates, and also the specific oscillation band of the changed flows.

Though the task design and target networks used in Kitaura et al. (2017) were not the same as the current study that aimed to examine the CON and FPN, it provided information about that the alpha- and theta-band oscillations may be involved to process additional task-set, i.e., single task compared with resting state. Also, a number of studies showed the increased alpha- and theta-band oscillations across the task in dual-task compared with single-task (Lin et al., 2011; Magosso et al., 2019; Sauseng et al., 2006; Shaw et al., 2019; Wang et al., 2018). This implied that the alpha- and theta-band oscillations may be influenced consistently for different situations that required handling an extra task-set. It may be related to the information flows between the substrates demanded by the set-maintenance demand, i.e., the CON and FPN. However, these studies did not effectively classify the specific function related to the alpha- and theta-band in previous dual-task studies. Yet, some insights were found in some dual-task design studies with time frequency analysis, which may show the amplitude of different oscillation frequency bands across time (e.g., Min & Park, 2010; Wang et al., 2018). Wang et al. (2018) used a dual-task design involving a driving task with calculation task. Hence, when the calculation task started, an extra task-set was required to be implemented and further processed. They applied time-frequency analysis (TFA) to explore the temporal information of varies oscillation bands. The results found a decreased alpha-band, but not theta-band, oscillation only after the onset of the calculation task. Hence, it was speculated that the alpha-band oscillation may be related to to information processing. In the current thesis, the time window of ERP components, SPN and N1, were used to define the time period of task-set implementation and information processing. The effect of different experimental conditions on the alpha- and theta-band oscillations were further verified with using TFA method across these two time periods. The information flow of the alpha- and theta-band oscillations could be then computed with ICoh analysis in order to investigate how the flows of oscillation activity during task-set implementation and information processing would be influenced by the distinct substrates of the CON and FPN.

2.7 Research Gaps

Previous studies discussed in Section 2.1 showed that the CON and FPN may work separately for set-maintenance control and rapid-adaptive control respectively. However, under higher set-maintenance demand (i.e., extra task-set in dual-task situations compared with single-task situations), only some substrates of the CON, i.e., aI/fO, dACC/msFC and aPFC, and FPN, i.e., dlPFC may find increased activation or increased connection between them. This implies that these substrates may play a more significant role in higher set-maintenance demand situations (see Section 2.2). In Section 2.3, it was further discussed that the changes of between-network functional connectivity were required to handle various types of task-set demands when contrasting to the resting-state functional connectivity. And the changes of between-network functional connectivity may contribute to explain the subsequent performance. It appears that the changes of functional connectivity of aI/fO of the CON and dlPFC of the FPN may be associated with subsequent performance. However, the effect of either the activation of aI/fO or dlPFC on the changes of functional connectivity has not been demonstrated in previous studies. Also, some of substrates in the CON (i.e., dACC/msFC and aPFC) were found to be more activated under a higher demand of set-maintenance. It was suggested that dACC/msFC and aPFC may be more involved to handle a higher demand of set-maintenance, such as handling two concurrent task-sets. However, the changes of connectivity of these two substrates did not find any association with subsequent performance during the lower set-maintenance demand. This implies that different neural substrates within the CON may alter their relationships with varying set-maintenance demand. It is yet to be known how the neural substrates of the CON may differentially influence subsequent performance. It is important to understand the underlying mechanism of the distinct substrates of CON on handling higher and lower demands of set-maintenance. In response to the abovementioned research gaps, this study was conducted in two phases with behavioural and electrophysiological methodology. Study One was a behavioural study conducted with TMS stimulation. It aimed to understand the different effects of the CON substrates on the subsequence performance on handling high set-maintenance demand. If the changes of functional connectivity were related to the facilitation of subsequent performance under high demand of set-maintenance, it was speculated that the facilitation effect of aI/fO would be stronger than dACC/msFC and aPFC.

The TMS stimulation may help to understand how the activation of a targeted substrate may causally influence the subsequent performance.

However, the behavioural design of Study One may not provide support to understand the changes of connectivity of the neural substrates. Besides, Study One mainly explored the differential effect of the CON substrates. In addition, further investigation is needed to examine how the CON interact with the FPN to handle higher and lower demands of set-maintenance and rapid-adaptive control. It was revealed in Chand and Dhamala's study (2017) that the CON may influence the FPN during the attention period, while the FPN may influence the CON during the decision-making period. It indicated that the changes of functional connectivity may shift from time-to-time based on different needs of the processes. Hence, the changes of functional connectivity should be investigated under specific periods of time. However, previous fMRI studies did not provide precise temporal information about the changes of functional connectivity between the CON and FPN. Different from fMRI studies, ERP studies could better reveal the temporal aspects of activations of different neural processes, which may be influenced by higher set-maintenance demand during different periods of time (see Section 2.4). The task-set implementation of set-maintenance control appeared to start 200ms earlier than the target stimulus onset while the information processing of rapid-adaptive control appeared around 150ms after the target stimulus onset. Hence, in Study Two, the changes of connectivity between the neural substrates of the dual network were examined during these two top-down controls, i.e., task-set implementation and information processing, while manipulating the higher and lower set-maintenance and rapid-adaptive demand.

In order to manipulate the demand of set-maintenance, single-task and dual-task design with the Flanker task and 2-back tasks were adopted. The details of the paradigm design are described in Section 3.2. A more sustainable task-set would be required in the 2-back tasks in that it needed to maintain and update task relevant information across the whole block of tasks. The 2-back tasks were used to demand the set-maintenance control across the tasks. On the other hand, the Flanker task tapped on the rapid-adaptive control. Under the incongruent trials, the rapid-adaptive demand was high, therefore, the target arrow was distracted by the incongruent peripheral arrow. It was more difficult to process the target information. Under the congruent trials, there was low rapid-adaptive demand as it was easier to process the target information without distraction information. Hence, there were two levels of set-maintenance demand and two levels of rapid-adaptive demand manipulated in order to provide four situations with different demands. The incongruent trials of the dual-task condition were regarded to be a more demanding situation that faced both high set-maintenance and rapid-adaptive demands. The changes of network connectivity were essential for handling the extra top-down control demand of set-maintenance and rapid-adaptive control. The changes of functional connectivity were expected to be more conspicuous in the incongruent trials of the dual-task condition. This design provided manipulation at the higher and lower demands of set-maintenance control and rapid-adaptive control. Therefore, it may help to understand how the changes of between-network connectivity of the CON and FPN may happen to handle various situations. The connectivity was measured by applying ICoh analysis in order to show the direction of the alpha- and theta-band oscillations flows among the dual network substrates (see Section 2.6). It may provide extra directional information on the functional connectivity change between the CON and FPN.

2.8 Objectives and Hypotheses

There were two studies in the current thesis. The objectives and hypotheses of Study One and Two are described below.

2.8.1 Study One – TMS Behavioural Study

1. Objective: To examine the differential effects of the iTBS-induced activation of three selected substrates of the CON, aI/fO, dACC/msFC and aPFC, on the enhancement of information processing performance, indicated by the difference between reaction time of the congruent and incongruent trials of the Flanker task, under the higher and lower demands of set-maintenance control, indicated by dual-task and single-task conditions.

For the objective of Study One, it was hypothesised that the reaction time of information processing performance would be significantly decreased after the iTBS stimulation was applied at aI/fO, but not at dACC/msFC and aPFC, under the dual-task condition.

2.8.2 Study Two – TMS EEG Study

1. Objective: To examine the differential effects of the iTBS-induced activation at the three substrates of the CON, aI/fO, dACC/msFC and aPFC, and two neural substrates of the FPN, i.e., dlPFC and dFC, on the enhancement on the reaction time of the Flanker task, under the higher and lower demands of set-maintenance control, indicated by the dual-task and single-task conditions, and higher and lower rapid-adaptive control, indicated by the congruent and incongruent trials.

2. a) Objective: To examine the differential effects of the iTBS-induced activation at the three substrates of the CON, aI/fO, dACC/msFC and aPFC, and two substrates of the FPN, dlPFC and dFC on the neural process during i) task-set implementation and ii) information processing, indicated by the amplitude of the SPN and N1 component respectively, under the higher and lower demands of set-maintenance control (i.e., single-task and dual-task conditions) and higher and lower rapid-adaptive control (i.e., congruent and incongruent trials).

2. b) Objective: To examine the differential effects between the activation, through iTBS stimulation, among the three substrates of the CON, aI/fO, dACC/msFC and aPFC, and two substrates of the FPN, dlPFC and dFC on the changes of effective connectivity during i) task-set implementation and ii) information processing under the higher and lower demands of set-maintenance control (i.e., single-task and dual-task conditions) and rapid-adaptive control (i.e., congruent and incongruent trials).

For Objective One of Study Two, it was hypothesised that a shorter reaction time of the Flanker task would be found after stimulating at aI/fO and dlPFC, but not at dACC/msFC, aPFC and dFC, under the incongruent trials of the dual-task condition.

For Objective 2a, it was hypothesised that i) the iTBS stimulation at aI/fO of the CON may facilitate the task-set implementation, as indicated by a more negative-going SPN component in the dual-task condition compared with the single-task condition compared to other CON substrates, i.e., dACC/msFC and aPFC, and FPN substrates, dlPFC and dFC. ii) iTBS stimulation at dlPFC of the FPN would facilitate the information processing as indicated by a less negative-going N1 component under the incongruent trials of the dual-task condition compared to the CON substrates, i.e., aI/fO, dACC/msFC and aPFC, and the FPN substrates, dFC.

For Objective 2b of Study Two, it was hypothesised that i) stimulation at aI/fO of the CON may lead to bidirectional flows of the theta-band oscillation found between aI/fO and dlPFC when handling high demanding situations. Also, it was hypothesised that the flows of the theta-band oscillation sent from aI/fO to the FPN substrates and also from dFC to the CON substrates would be apparent. For the information processing period, it was hypothesised that ii) stimulation at dlPFC of the FPN may increase the effective connectivity of alpha-band oscillation under the higher demand of set-maintenance and rapid-adaptive. First, the aI/fO and dlPFC may have bidirectional flows of the alpha-band oscillation found. Also, there should be increased information flows of the alpha-band sent from aI/fO to the other substrates within CON and sent from dlPFC to the FPN substrates.

CHAPTER THREE

METHODOLOGY OF BEHAVIOURAL AND ELECTROENCEPHALOGRAPHY (EEG) STUDY

3.1 Overview of Study One – TMS Behavioural Study

In order to examine the effect of different network members of the CON on top-down control, the Behavioural Study aimed to investigate how activation of the different neural substrates of the CON by using the iTBS stimulation may differentially influence cognitive task performances under various set-maintenance and rapid-adaptive demands.

The results of previous studies suggested that the neural substrates (or members) within cortical networks are more connected functionally with other members (Cole et al., 2013; Dosenbach et al., 2008; Gordon et al., 2018). They may influence the functionality of the network more than other members (Cole et al., 2013; Gordon et al., 2018). The dlPFC of the CON showed a robust role on different aspects of top-down control compared with nodes (Chand & Dhamala, 2017). However, rare studies have explored how the substrates of the CON, aI/fO, dACC/msFC and aPFC may differentially influence the top-down set-maintenance control. Before exploring the network connectivity, when using the iTBS stimulation, this behavioural Study One aimed to investigate the differential effect of the activation of the CON substrates, aI/fO, dACC/msFC and aPFC, on the sequence task performance in single dual cognitive tasks which were handling different set-maintenance and rapid-adaptive demands.

3.2 Methods of Study One – TMS Behavioural Study

3.2.1 Subjects

Thirteen right-handed participants (7 females; mean age = 26.5 years; SD = 4.1 years; range = 20 – 34 years) were recruited with a convenient sampling method. The inclusion criteria aimed to ensure intact cognitive functions, mainly the set-maintenance and rapid-adaptive control functions, and they are listed as below:

(1) aged between 18 to 35;

(2) had obtained the interference score of 50 and error score of two or less in the Stroop Test (Chinese version) (Franzen, 1987; Stuss et al., 2001; Van der Elst et al., 2006; Wang et al., 2018);

(3) had obtained the perseverative errors of 9 and non-perseverative errors of 10 in the Wisconsin Card Sorting Test (WCST; Axelrod et al., 1992; Barceló et al., 2000; Gunner et al., 2012);

(4) had obtained the reaction time of 90 in the Color Trails Test-I (CTT-I) and the reaction time of 200 in CTT-II (D'Elia et al., 1996; Nielsen et al., 2018);

(5) had obtained the digit span of the 4 items in the Digit Span Test- Backward (DST-B; Leung et al., 2011; Waters & Caplan, 2003).

The exclusion criteria included through self-report, (1) perceptual deficits (e.g., colour blindness), (2) neurotic (e.g., depression) or psychotic disorders (e.g., schizophrenia), and (3) neurological conditions (e.g., stroke and Parkinson's disease).

3.2.2 Neuropsychological Tests

Stroop Test was mainly used to measure conflict solving ability, which related to the rapid-adaptive control network (Stuss et al., 2001; Vanderhasselt et al., 2009). In the test, there are three parts including word reading (WR), colour naming (CN) and incongruent colour naming (INC). In the WR part, one hundred Chinese words of the colour names, including "紅" [red], "藍" [blue], "綠" [green] and "黃" [yellow], were printed in black on a white background. They were arranged in a 10 x 10 manner. All of the colour names were shown to the participants and they were required to read the words out as quickly and precisely as possible, with the sequence from top to bottom, left to right. In the CN part, a one hundred coloured square box, including red, blue, green, and yellow, were printed on a white background. These boxes were arranged in a 10 x 10 manner. All of the colour boxes were shown to the participants and they were required to read the words out as quickly and accurately as possible, with the sequence from top to bottom, left to right. In the INC part, four types of Chinese colour names (i.e., "紅"

[red], “藍” [blue], “綠” [green], “黃” [yellow]) were printed in colour on a white background but the colours of the words were not matched with the meaning of the words themselves. One hundred coloured words were arranged in a 10x10 manner. All of the colour names were shown to the participants and they were required to read out the words as quickly and precisely as possible, with the sequence from top to bottom, left to right. In all three parts, the times taken were recorded with a digital timer and the number of errors were counted. The scores were computed with the same method as former studies (Stuss et al., 2001). The high reliability of the Stroop Test was demonstrated with high test-retest reliability coefficient of WR, CN, and INC, which were 0.831, 0.738, and 0.671 respectively (Franzen, 1987).

***Wisconsin Card Sorting Test* (WCST)** was used to examine the set-shifting ability associated with set-maintenance control function (Barceló et al., 2000). Four cards were presented to each participant who needed to match the fifth card to one out of the previous four cards. On each of the cards, a different number of different symbols with different colours were printed. The participants needed to match the cards with one out of three possible criteria, including number, shape, or colour of the symbols, while the criteria were not told to them before the trials. There was feedback, either right or wrong, provided after each trial. The participants were required to explore the correct criteria themselves based on this feedback. The criteria were changed every 10 trials and the participants were required to explore the new criteria again. The perseverative errors and non-perseverative errors were recorded. The corresponding test-retest reliability coefficient of the perseverative errors and non-perseverative errors were 0.97 and 0.75 respectively (Axelrod et al., 1992).

Color Trails Test (CTT) was used to ensure the selective attention ability of the participants in the study (D'Elia et al., 1996). There are two parts, CTT part 1 (CTT-1) and part 2 (CTT-2). For CTT-1, a line was required to be drawn in order to join 25 coloured circles in ascending order from 1 to 25 based on the digit inside each of the coloured circles. For CTT-2, besides the rule of CTT-1, coloured circles needed to join the 25 circles alternatively between pink and yellow. In both CTT-1 and CTT-2, the participants were told to finish as fast and accurately as possible. The times of completion for each part were recorded with a digital timer. The test-retest reliability of the CTT-1 and CTT-2 were reported as 0.64 and 0.79 respectively (D'Elia et al., 1996).

Digit Span Test-Backward **(DST-B)** was used for testing the working memory ability (Waters & Caplan, 2003). Each respondent first listened to a digit span which may have consisted of 4-7 digits and was then required to repeat the digit span in reverse order. The number of correct trials were recorded. The test-retest reliability of the DST-B was reported to be 0.65 (Waters & Caplan, 2003)

3.2.3 Experimental Procedure

Before signing the consent form, each participant was explained the aim and the procedure of the experiment. The participants were then instructed to finish a demographic questionnaire (including name, age, education level, and medical record), the TMS screening form (Keel et al., 2001) and four neuropsychological tests (i.e., the Stroop Test, the WCST, the CTT, and the DST-B). Afterwards, the resting threshold determination of the TMS stimulation was measured with a standardised procedure (see Section 3.2.6 for details).

For the study design, TMS stimulations were given at four sites of the scalp corresponding to three network members of the CON, including aI/fO, dACC/msFC, and aPFC, and a control site, the vertex. All of the stimulations were in a randomised order. In order to minimise the carry-over effect of the previous stimulation, each stimulation was separated for at least 24 hours. Before and after the stimulation at each site, each participant was required to finish 4 pseudo-randomised blocks of cognitive tasks, including 2 blocks of single-task condition (i.e., Flanker task only with congruent and incongruent conditions) and 2 blocks of dual-task condition (i.e., both the Flanker task and detection task). Thus, a design of 2 task effect (i.e., single- and dual-task conditions) × 2 congruency effect (i.e., congruency and incongruency trials) × 2 stimulation effect (i.e., before and after stimulation) per site stimulation was adopted in this study.

3.2.4 Experimental Paradigm of the Single- and Dual-Tasks

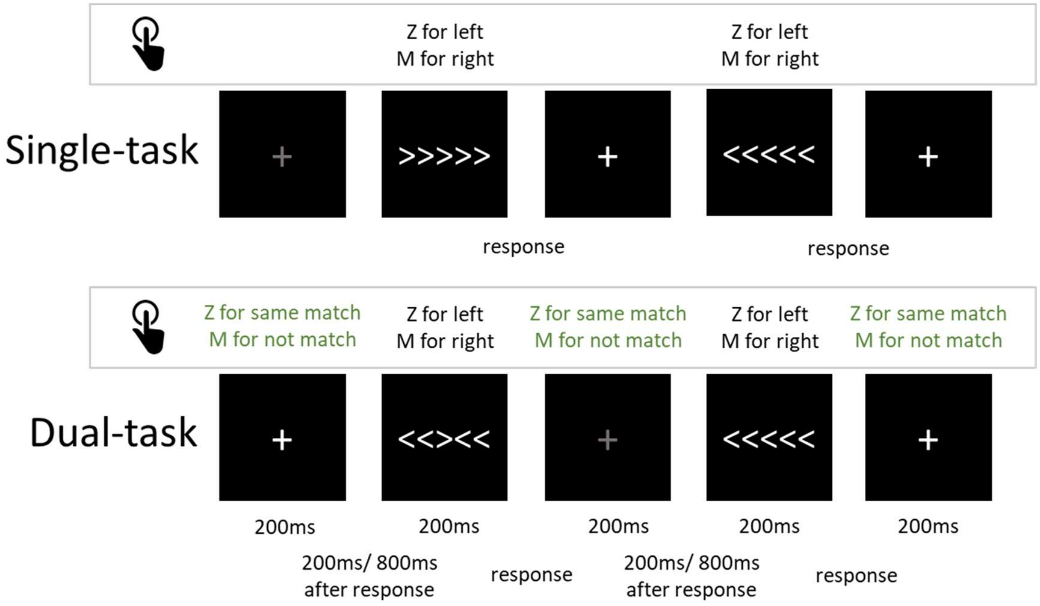
4.2.4.1 Single-task Condition with Flanker Task. The paradigm of the single- and dual-task was shown in Figure 3.2 (p. 46). Each trial started with a fixation cross presented at the centre of the black screen (resolution: 1366 × 768 pixels) for 200ms, and it was either in white or grey colour, of which each participant disregarded. After a blank screen was presented for either 200ms or 800ms (pseudo-randomised with 1:1 ratio), five arrows (">" or "<") were presented horizontally at the centre for 200ms. The orientation of the five arrows were presented in either a congruent or incongruent manner. In the congruent trials, all five arrows pointed to the same direction. In the incongruent trials, the pointing direction of the middle arrow was opposite to that of the other four. Within a 3000ms time limit, the participants were required to decide the pointing direction of the middle arrow disregarding the colour of the fixation cross. He or she needed to press a left button, "Z" key with their left forefinger if the middle arrow pointed to the left, or to press a right button "M" key, with their right forefinger if the middle arrow pointed to the right.

3.2.4.2 Dual-task Condition with Flanker and 2-Back Tasks. In the dual-task condition, apart from the Flanker task, each participant was engaged concurrently in 2-back tasks (see Figure 3.2, p. 46). The timings of stimuli in the dual-task condition were the same with those in the single-task condition. A white or grey fixation across (200ms) was first presented as in the single-task condition. Within a 3000ms time limit, the participants were then required to determine whether the colour of the fixation across attended was the same with that of the fixation cross showed two trials before. He or she was required to press “Z” with their left forefinger and “M” with their right forefinger if the two fixation crosses were the same and different, respectively. A blank screen (either 200ms or 800ms) was then presented after the response of the participants. Five congruent or incongruent arrows were shown (200ms) as in the single-task condition. The participants were required to respond to the concurrent Flanker task by pressing “Z” with their left forefinger and “M” with their right forefinger for the left or right middle arrow, respectively.

Each block of both the single- and dual-task conditions consisted of 64 trials, 32 congruent and 32 incongruent trials. There were, hence, 64 trials for each of the 8 conditions. The presentation timing of the stimuli and the responses of the participants were recorded by the stimulus presentation program, STIM^2 (NeuroScan Labs, Sterling, VA).

Figure 3.2

The Experimental Paradigm of the Single-Task and Dual-Task Conditions



Note. A 200ms fixation cross was first presented at the centre. For the single-task condition with a Flanker task, the participants were required to determine the direction of the middle arrow which was sandwiched by 4 peripheral arrows in either a congruent or congruent condition (200ms) after either a 200ms or 800ms blank page. The participants were required to decide on the direction of the middle arrow by pressing button "Z" for left or "M" for right. For the dual task, besides the Flanker task, the participants needed to concurrently perform 2-back tasks, required to determine whether the fixation cross (200ms) was the same or different with the fixation showed two trials before by pressing button "Z" or "M" on a keyboard, respectively.

3.2.5 Transcranial Magnetic Stimulation (TMS)

The figure-of-eight coil (Cool-B65) (MagPro X100, MagVenture, Farum, Denmark) was used for the TMS stimulation. It is able to deliver stimulations with high repetitive pulses without overheating. The transducer head of the coil is 1.8-kilogramme-weight with a dimension of 172 x 92 x 51 mm and links with a 2-metre-long cable. The outer and inner diameters of the coil are 75 mm and 35mm respectively. The maximum dB/dt is 36 kT/s near the coil surface and the maximum active pulse width is 290µs.

Intermittent theta-burst transcranial magnetic stimulation (iTBS) was used for the TMS protocol of the current study. The iTBS was shown to reliably and potently facilitate brain activities at both motor- (Chung et al., 2016) and cognitive-related (Lowe et al., 2018) cortical regions. During each iTBS stimulation, there were 20 chains of TBS pulses with an interval of 8000ms. Each chain of the TBS pulses contained 30 pulses, which consisted of three consecutive 50 Hz pulses repeating 10 times at 5Hz. Each of the stimulations, hence, included of total of 600 pulses.

3.2.6 Determination of Motor Threshold

The intensity of the iTBS pulses was set at 80% of the determined motor threshold. The determination of the motor threshold was based on the standardised procedure reported by Sandrini and colleagues (2011). The TMS coil firstly moved around the scalp region corresponding to the right primary motor area (M1) and delivered single pulse stimulation. The M1 was identified when there was an observable muscle contraction of the left first dorsal interosseous (FDI) after the stimulation. The optimal location was determined until all of the 10 single pulse stimulations consistently elicited the contraction of the left FDI. The motor threshold was then determined by descending the intensity of the single pulse stimulation at the optimal location until the FDI contractions were elicited in 5 out of 10 trials (Sandrini et al., 2011).

3.2.7 Selected Stimulation Sites

Four stimulation sites were targeted. Three sites were within the CON, i.e., the aI/fO (MNI: 36, 16, 4; Gratton et al, 2013, 1014), dACC/msFC (MNI: 6, 15, 67; De Ridder et al., 2011) and aPFC (MNI: 27, 50, 23; Chen, 2013) while the other one was control stimulation site, i.e., the vertex (MNI: 5, -25, 74; Kehrer et al., 2015). The iTBS was applied to four target sites in a randomised order to neutralise the site stimulation effect. In order to keep the reliability of the stimulation locations, a frameless stereotactic neuronavigation system (TMS Navigator, Localite) was used to provide the real-time location of the cortical surface corresponding to the stimulation targets.

3.2.8 Data Analysis

The congruency effect was first calculated by subtracting the reaction time of each congruent trial from that of each incongruent trial. Stronger congruency effect was defined as a longer time was needed to handle moment-to-moment conflict situation (Egner, 2007; Weinbach & Henik, 2012), which may represent less effective rapid-adaptive control. The subtracted reaction time was then submitted to a three-way repeated measures ANOVA model of stimulation effect (before and after stimulation) × set-maintenance conditions (single- and dual-task trials) × stimulation sites (aI/fO, dACC/msFC, aPFC and vertex). The significant level of the main and interaction effects of simulation, set-maintenance, and rapid-adaptive conditions were set to be 0.05. The Greenhouse-Geisser corrections were applied when the assumption of sphericity was violated. All statistical data analyses were conducted with the SPSS software (Version 25.0).

3.3 Overview of Study Two – TMS EEG Study

Though Study One may have provided extra information about the effect of the CON on subsequent top-down control performance, it is yet to be understood how the CON and FPN may interact, via within- and between-network connectivity, in order to handle different top-down control demands during different time periods of control processes. Using the TMS and EEG methods, Study Two aimed to investigate how the activation of substrates of the CON and FPN may have influenced the within- and between-network connectivity during task implementation and the information processing period.

3.4 Methods of Study Two – TMS EEG Study

3.4.1 Subjects

Eighteen right-handed participants (8 females; mean age = 25.3 years; SD = 4.9 years; range = 18-34 years) were recruited via convenient sampling. The inclusion criteria and exclusion criteria were the same as Study One (see Section 3.2.1 for details).

3.4.2 Neuropsychological Tests

Please refer to Section 3.2.2 for details.

3.4.3 Experimental Procedure and Design

Before signing the consent form, each of the participants was explained the aim and the procedure of the experiment. The participants were then instructed to finish a demographic questionnaire (including name, age, education level, and medical record), the TMS screening form (Keel et al., 2001) and four neuropsychological tests (i.e., the Stroop Test, the WCST, the CTT, and the DST-B).

After finishing the screening, the participants needed to first go through the setup of the EEG followed by determining the motor threshold of the TMS (see Section 3.2.6 for details).

Before the stimulation, the rules of the three types of cognitive tasks, both single (i.e., either the Flanker task or the 2-back tasks only) and dual task (i.e., both the Flanker task and detection task simultaneously), were explained to the participants. He or she needed to finish the six training blocks, including two times for all three types of tasks, in an electromagnetically shielded and distraction-free chamber.

The participants were then arranged to sit on an armchair for the iTBS stimulation procedure (see Section 3.2.5 and 3.2.6 for details). The iTBS intensity was set as 80% of the motor threshold. In Study Two, the stimulations were applied at six target sites, including three sites of the CON (i.e., dACC/msFC, aI/fO and aPFC), two sites of the FPN (i.e., dlPFC and dFC), and one control site (i.e., the vertex). The six target sites were stimulated in randomised order on two separated days. Three stimulations were conducted on each day. After each stimulation, the participants needed to finish a total six blocks of tasks, including two blocks of single-task condition with the Flanker task, single-task condition with 2-back tasks, and dual-task condition with both the Flanker task and detection task based on the instructed rules. Each of the stimulations were separated by at least 90 minutes to minimise the carry-over effect of the previous stimulation. All of the EEG signals were recorded during the tasks.

3.4.4 Experimental Paradigm

3.4.4.1 Single-task Condition with Flanker Task. See Section 3.2.4 for details.

3.4.4.2 Single-task Condition with 2-Back Tasks. Similar with the stimuli of the Flanker task, a white or grey fixation across (200ms) was presented. Within a 3000ms time limit, the participants were then required to determine whether the colour of the fixation across attended was the same with that of the fixation cross showed two trials before. He or she was required to press "Z" with their left forefinger and "M" with their right forefinger if the two fixation crosses were the same and different, respectively. A blank screen (either 200ms or 800ms) was presented after the response of the participants. Five congruent or incongruent arrows were then shown (200ms). The participants were required not to respond to the arrows and wait until the next trials was shown.

3.4.4.3 Dual-task Condition with Flanker and 2-Back Tasks. see Section 3.2.4 for details.

3.4.5 iTBS Stimulation

The procedural of iTBS stimulation was the same as the Behavioural Study (see Section 3.2.5 and 3.2.6 for details). The only difference was that there were six target TMS stimulation sites, including three sites of the CON, the right dACC/msFC (MNI: 6, 15, 67; De Ridder et al., 2011), right aI/fO (MNI: 36, 16, 4; Gratton et al., 2013, 1014) and right aPFC (MNI: 27, 50, 23; Chen, 2013); two sites of the FPN, right dlPFC (MNI: 42, 30, 41; Kehrer et al., 2015) and right dFC (MNI: 41, 3, 36; Dosenbach et al., 2006); and one control stimulation site at the vertex (MNI: 5, -25, 74; Kehrer et al., 2015).

3.4.6 Electroencephalography (EEG) Recordings and Offline Data Processing

In the sound-proof chamber, the EEG signals were magnified by the head-box of the SynAmps2 Digital DC EEG Amplifier and recorded by 64 channels of 6mm-diameter-width Ag/AgCl electrodes (Brain Products). They were mounted on a BrainCap for TMS (Brain Products). The sampling rate were set at 1,000 Hz. The reference electrodes were located at the left and right mastoids while the ground electrode was in front of the AFz electrode. Impedances of all electrodes were kept at or below 5kΩ during the recordings. The timing of the onset of all stimuli outputs and responses of the participants were recorded via the synchronisation of the stimulus presentation programme, $STIM^2$ (NeuroScan Labs, Sterling, VA). The EEGs were recorded across all the experimental tasks.

An offline pre-processing procedure was conducted with the Curry Neuroimaging Suite 7 software (Compumedics Neuroscan, Charlotte, NC). The electrophysiological data of each electrode site was re-referenced to the average of the left and right mastoid electrodes. A 1- 30 Hz band filter was applied to the re-referenced signals. The blink-related eye artifacts were then reduced using the regression algorithm in the Curry software.

3.4.7 Data Analysis

3.4.7.1 Behavioural Data.

The reaction time of the Flanker task was submitted to a three-way repeated measures ANOVA model of task conditions (single- and dual-task trials) × congruency (congruent and incongruent trials) × stimulation sites (aI/fO, dACC/msFC, aPFC, dlPFC, dFC and vertex). The significant level of main and interaction effects of simulation, set-maintenance and rapid-adaptive conditions were set to be 0.05. The Greenhouse-Geisser corrections were applied when the assumption of sphericity was violated. All statistical data analyses were conducted with the SPSS software (Version 25.0).

3.4.7.2 ERP, TFA and Isolated Coherence Analysis (ICoh).

3.4.7.2.1 Electroencephalography (EEG) Recordings and Offline Data Processing. In the sound-proof chamber, EEG signals were recorded with 64 channels of 6mm-diameter-width Ag/AgCl electrodes (Brain Products) and all singles were amplified by the head-box of the SynAmps2 Digital DC EEG Amplifier. All electrodes were fixed on a BrainCap for TMS (Brain Products). The sampling rate was set at 1,024 Hz. The reference electrode and the ground electrode were located at the left and right mastoids, and in front of the AFz electrode respectively. The configuration of the electrode positions was defined at the SynAmps2 Digital. Impedances of all the recording electrodes were kept at or below 5kΩ during the recordings. The timings of all stimuli onset outputs were recorded via the synchronisation of the stimulus presentation programme, STIM2 (NeuroScan Labs, Sterling, VA). The EEGs were recorded across all the experimental tasks. An offline pre-processing procedure was conducted using the Curry Neuroimaging Suite 7 software (Compumedics Neuroscan, Charlotte, NC). The electrophysiological data, for all electrode sites, was re-referenced to the average of the left and right mastoid reference electrodes. The re-referenced signals were then digitally filtered to the 1- 30 Hz band. Then, the blink-related eye artifacts were reduced using the regression algorithm in the Curry software. For each channel, medians and median absolute deviations were computed for the ERP amplitude and spectral power in the alpha (8-12Hz) and beta (4-8Hz) bands for two defined time windows, from -200 to 0ms of stimulus onset, and from 150 to 300ms of stimulus onset. Independent component analysis (ICA) was applied on the grand-averaged waves to confirm the ERP component when using the Curry Neuroimaging Suite 7 software (Compumedics Neuroscan, Charlotte, NC).

3.4.7.2.2 ERP Analysis for the SPN and N1. Statistical analyses were conducted on the ERP mean millisecond amplitudes obtained within successive measurement windows relative to a 500-msec prestimulus baseline. The analyses included EEG data from only the correct trials across higher and lower set-maintenance demands (dual-task and single-task), and higher and lower rapid-adaptive demands (congruent and incongruent) after stimulating at different targeted sites (three sites of the CON: aI/fO, dACC/msFC, and aPFC; two sites of the FPN: dlPFC and dFC; and the control site: the vertex). ERP mean amplitudes were obtained within the SPN (-200 – 0ms) at Fz, and N1 (150 – 300ms) at Pz. The obtained mean amplitude difference was calculated by subtracting the mean amplitude after stimulating at the vertex from the mean amplitude after stimulating at each of the five other targeted sites.

The mean amplitude difference was submitted to a three-way repeated measures ANOVA model of task conditions (single- and dual-task trials) × congruency (congruent and incongruent trials) × stimulation sites (three sites of the CON: aI/fO, dACC/msFC, and aPFC; two sites of the FPN: dlPFC and dFC). The significant level of the main and interaction effects of the simulation, set-maintenance, and rapid-adaptive conditions were set to be 0.05. The Greenhouse-Geisser corrections were applied when the assumption of sphericity was violated. All statistical data analyses were conducted with the SPSS software (Version 25.0).

3.4.7.2.3 Time-Frequency Analysis (TFA). The EEG data of correct trials was further decomposed into the power spectrum of different oscillation frequency across time. It may help to ensure the effect of the iTBS on the theta-band and alpha-band oscillations at specific period of time, task-set implementation and information processing period, before the ICoh analysis. The analysis included all the correct trials under dual-task and single-task condition (i.e., higher and lower set-maintenance demands), congruent and incongruent trials (i.e., higher and lower rapid-adaptive demands), and six targeted stimulation sites (three sites of the CON: aI/fO, dACC/msFC, and aPFC; two sites of the FPN: dlPFC and dFC; and the control site: the vertex). For the TFA, the event-related spectral perturbation (ERSP) was computed as the power spectrum of each epoch, that was normalized by the respective mean baseline spectra. After correcting the baseline period which was from −500 to −200 ms, the power was then averaged and converted to log power based on the following formula:

$$\text{ERSP}\ (f,t) = \frac{1}{n}\sum_{k=1}^{n}(F_k(f,t)^2)$$

Here, n is the number of trials, and F_k (f, t) is the spectral estimation of the k^{th} trial at frequency f and time t.

The ERSP was obtained within two of time windows, -200 – 0ms and 150 – 300ms, based on the ERP analysis at Fz. Then, the extracted ERSPs were submitted to five separated three-way repeated measures ANOVA model of task conditions (single- and dual-task trials) × congruency (congruent and incongruent trials) × stimulation sites (aI/fO and vertex; dACC/msFC and vertex; aPFC and vertex; dlPFC and vertex; and dFC and vertex). All of the ERSP data was processed by using EEGLab (Delorme and Makeig, 2004) and custommade Matlab scripts. The significant level of the main and interaction effects of the simulation, set-maintenance, and rapid-adaptive conditions were set to be 0.05. All statistical data analyses were conducted with the SPSS software (Version 25.0).

3.4.7.2.4 Isolated Coherence Analysis (ICoh). The ICoh is a multivariate autoregressive model suggested by Pascual-Marqui et al. (2014). Referring to Pascual-Marqui et al. (2014), the equation representing ICoh (derived in the frequency domain) are expressed as the following:

$$k_{i\leftarrow j}(w) = \frac{S_{\varepsilon_{ii}}^{-1}\left|\breve{A}(\omega)_{ij}\right|^2}{S_{\varepsilon_{ii}}^{-1}\left|\breve{A}(\omega)_{ij}\right|^2 + S_{\varepsilon_{jj}}^{-1}\left|\breve{A}(\omega)_{jj}\right|^2}$$

satisfying the normalisation condition: $0 \leq k_{i\leftarrow j}(\omega) \leq 1$ (Pascual-Marqui et al., 2014). Here, $k_{i\leftarrow j}(\omega)$ signifies the ICoh value that the regions of interest (ROIs) j influences ROI i at a given frequency ω. For the matrix $\breve{A}(\omega) = I - A(\omega)$, it relates to the matrix A(ω) derived by the least square fitting with I being the unit matrix of order N. The matrix $S\varepsilon$ is the covariance of the residual errors of the multivariate autoregressive model. All of the ICoh analyses were conducted by a free academic software package available at http:// www.uzh.ch/keyinst/loreta.htm.

3.4.7.2.5 Selected regions of interests (ROIs). In order to examine effective connectivity across the substrates between the CON and FPN, a total of six ROIs were selected and their MNI coordinates were based on those reported in Dosenbach et al. (2006). The ROI included the three substrates in the CON, right aI/fO (MNI: 36, 16, 4), dACC/msFC (MNI: 6, 15, 67) and right aPFC (MNI: 27, 50, 23), and the three substrates in the FPN, right dlPFC (MNI: 42, 30, 41), right dFC (MNI: 41, 3, 36) and right IPS (MNI: 30, -61, 39).

Statistical tests were performed based on the method of nonparametric randomisation of the maximum statistic. It may correct multiple testing whilst not relying on the assumption of any specific or exact statistical distribution. With statistical nonparametric mapping (SnPM), surrogate permutations (5,000 in the current study) are created rendering a histogram which provides the statistical threshold (Pascual-Marqui et al., 2014). The causal effective connectivity was computed for six regions of interest including three CON substrates: dACC/msFC, aI/FO, and aPFC, and three FPN substrates: dlPFC, dFC, and IPS for each of two frequency bands, i.e., alpha- and theta-band oscillations across for task conditions, i.e., congruent trials of single-task condition, congruent trials of dual-task condition, incongruent trials of single-task condition and incongruent trials of dual-task condition. The significant level of connectivity analysis was set to be 0.05.

CHAPTER FOUR

RESULTS

4.1 Results of Study One

4.1.1 Demographic Data

Thirteen participants (male = 6; mean age = 26.5 years; SD = 4.1 years) were recruited by snowball sampling. All of them fulfilled the inclusion criteria. One had secondary education while the rest had undergraduate university education. Nine had a full-time job while four were students. Table 4.1a (p. 63) summarises the demographic data of the 13 participants of Study One. For the score of neuropsychological screening test, the word reading, color naming and incongruent color naming score of Stroop Test were 35.78s, 48.49s and 65.88s respectively with mean interference score below 20s. Also, the average self-correction score was below 1. It indicated that the conflict solving ability, which related to rapid-adaptive control function, was within the inclusion criteria. For the perseverative errors and non-perseverative errors of WCST, the scores obtained were 3.39 and 5.72 (the cutoff scores were 9 and 10, respectively). It implied the set-shifting ability of set-maintenance control was intact. The reaction time of CTT I and CTT II was found 35.78s and 48.49s respectively. It showed the selective attention ability of rapid-adaptive control fulfil the inclusion criteria of 90 s and 200s for CTT I and CTT II respectively. And for the DST-B, the average score of recorded digit span met 6.83 which is above the cutoff score 4. It showed the intact working memory of the participants. Table 4.1b (p. 64) summarises the neuropsychological screening test of them.

Table 4.1a

Demographics of the 13 participants of Study One

Male (%)	6 (46.2)
Age (SD) (years)	26.5 (4.1)
Educational Level (%)	
Secondary	1 (7.7)
Undergraduate	12 (92.3)
Employment state (%)	
Full-time	9 (69.2)
Student	4 (30.8)

Note. SD = standard deviation.

Table 4.1b

Test scores of the screening neuropsychological tests of the participants of Study One

Stroop Test	
Word Reading	
Total Time (second)	35.78 (14.18)
Self-correction	0.5 (0.71)
Color Naming	
Total Time (second)	48.49 (10.23)
Self-correction	0.94 (0.87)
Incongruent Color Naming	
Total Time (second)	65.88 (14.79)
Self-correction	0.67 (0.84)
Difference Score	
IN – WR (second)	12.71 (17.07)
IN – CN (second)	17.39 (11.31)
Wisconsin Card Sorting Test	
Perseverative errors	3.39 (1.38)
Non-perseverative errors	5.72 (1.71)
Color Trails Test	
Color Trails Test-I (second)	35.78 (14.18)
Color Trails Test-II (second)	48.49 (10.23)
Digit Span Test- Backward	
Digit span	6.83 (0.38)

Note. Standard deviations are in parentheses ( )

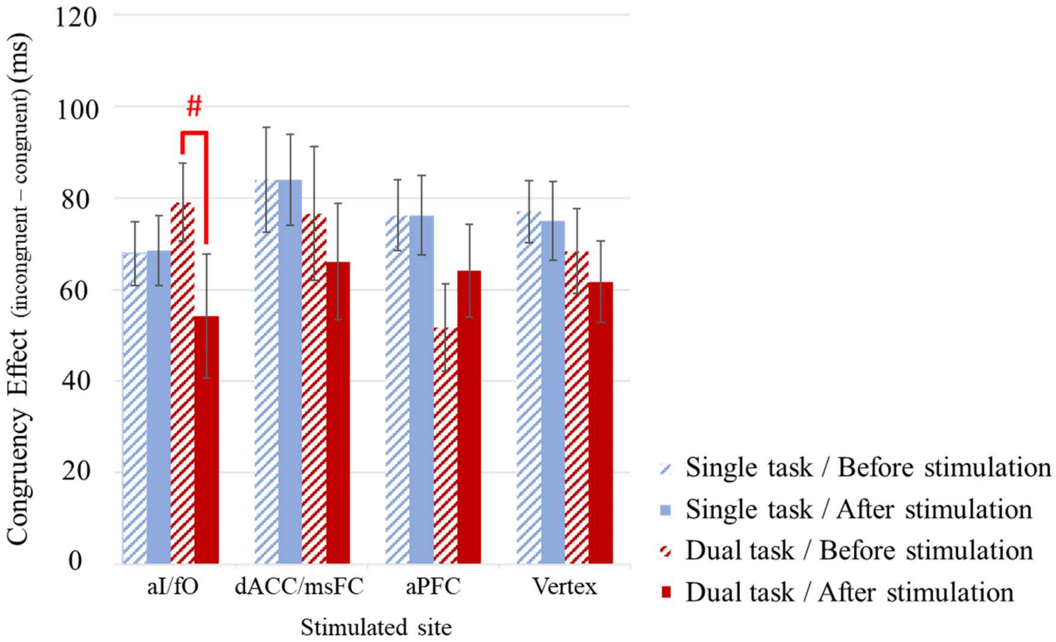
4.1.2 Behavioural Results

Study One aimed to investigate how the iTBS-induced activation of the substrates of the CON (i.e., dACC/msFC and aPFC) under various set-maintenance demands, may differentially influence the rapid-adaptive top-down control performance, in terms of the congruency effect. The congruency effect was computed by subtracting the reaction time of congruent trials from that of incongruent trials. The three-way ANOVA of stimulation effect (before and after stimulation) × task conditions (single- and dual-task conditions) × stimulation sites (aI/fO, dACC/msFC, aPFC and vertex) revealed significant interaction stimulation effect × set-maintenance effect × stimulation sites interaction ($F_{3,36} = 3.18$, $p = 0.036$). Post-hoc tests of two-way repeated measures ANOVA revealed the marginally significant interaction of stimulation effect × task conditions when the iTBS was applied at aI/fO ($F_{1,12} = 4.26$, $p = 0.061$, see Figure 4.1a, p. 67) only but did not reveal significant results at the other cortical sites, i.e., ACC/msFC, aPFC, and the vertex ($p > 0.1$). This interaction effect showed the congruency effect after the iTBS stimulation at aI/fO ($M = 79.09$s, $SD = 30.88$s) was marginally reduced when compared with that before the iTBS stimulation ($M = 54.28$s, $SD = 48.86$s) under the dual-task condition ($t_{12} = 2.15$, $p = 0.053$), but the difference of the congruency effect between before ($M = 67.85$s, $SD = 24.98$s) and after ($M = 68.46$s, $SD = 27.62$s) stimulation at aI/fO was not found in the single-task condition ($t_{12} = -0.13$, $p = 0.90$).

To further investigate the effect of stimulation at aI/fO on the congruency effect in dual-task condition, the reaction time of the congruent and incongruent trials were separated and submitted to another two-way repeated measures ANOVA model of stimulation effect (before and after the iTBS stimulation) × rapid-adaptive conditions (congruent and incongruent trials) was conducted with the reaction time. The results revealed marginally significant interaction effect of stimulation effect × rapid-adaptive conditions ($F_{1,12} = 4.61$, $p = 0.053$). Post-hoc tests of paired sample t-test revealed significant shorter reaction time for the incongruent trials after the iTBS stimulation at aI/fO ($M = 474.05$s, $SD = 77.42$s), compared with that before the iTBS stimulation at aI/fO ($M = 510.41$s, $SD = 96.99$s) ($t_{12} = 3.42$, $p = 0.005$, see Figure 4.1b, p. 67). For the congruent trials condition, there were no significant difference found between the reaction time in the Flanker task before ($M = 431.32$s, $SD = 71.16$s) and after ($M = 419.78$s, $SD = 67.34$s) iTBS stimulation at aI/fO ($t_{12} = 1.27$, $p = 0.227$). Table 4.1c (p. 68) shows the mean reaction time of the Flanker task across task conditions (dual-task and single-task condition) and congruency (congruent and incongruent trials) before and after stimulating at different cortical sites, i.e., aI/fO, dACC/msFC, aPFC, and the vertex.

Figure 4.1a

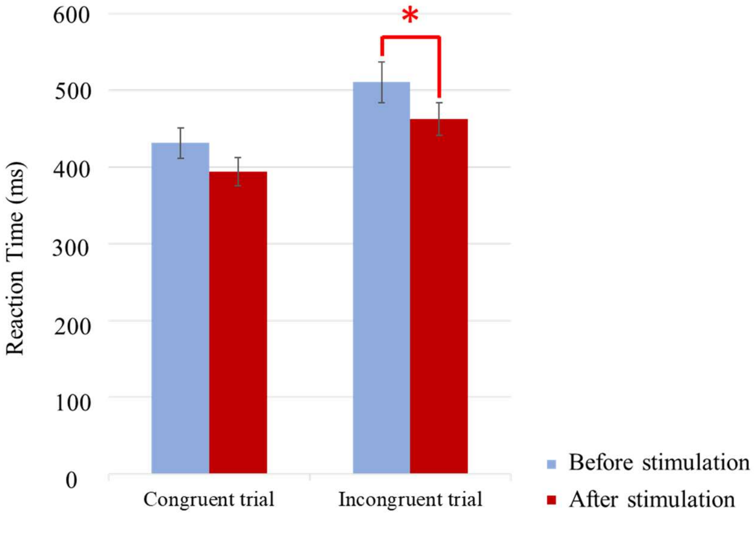
The Congruency Effect of the Flanker Task across Task Conditions before and after iTBS Stimulation



Note. # < 0.1, total number *N* = 13, the error bars represent the standard error of the mean

Figure 4.1b

The Reaction Time of Flanker Task across Task conditions after Stimulating at aI/fO



Note. * < 0.01, total number *N* = 13, the error bars represent the standard error of the mean

Table 4.1c

Reaction time (mean and standard deviations) in tasks with different conditions (dual-task and single-task conditions) and congruency (congruent and incongruent trials) before and after stimulating at the four different cortical sites, i.e., aI/fO, dACC/msFC, aPFC and the vertex

Mean reaction time of Flanker task across different top-down control conditions under iTBS applications at different CON sites

		Dual-task condition (ms)			Single-task condition (ms)		
		Congruent trials	Incongruent trials	Congruency score	Congruent trials	Incongruent trials	Congruency score
		Stimulation at the CON sites					
aI/fO	Before stimulation	431.32 (71.16)	510.41 (96.99)	79.09 (30.88)	394.51 (58.4)	462.37 (66.46)	67.85 (24.98)
	After stimulation	419.78 (67.34)	474.05 (77.42)	54.28 (48.86)	393.92 (50.84)	462.38 (63.69)	68.46 (27.62)
dACC/msFC	Before stimulation	459.46 (71.8)	536.06 (91.63)	76.6 (52.72)	401.69 (43.68)	485.67 (51.26)	83.98 (40.98)
	After stimulation	461.1 (53.78)	527.17 (80.08)	66.07 (45.81)	415.52 (78.08)	497.68 (93.29)	82.16 (36.02)
aPFC	Before stimulation	457.48 (128.69)	509.2 (122.98)	51.72 (34.43)	406.54 (53.73)	482.79 (69.19)	76.25 (28.21)
	After stimulation	424.42 (64.85)	488.48 (84.89)	64.06 (36.6)	395.02 (41.41)	467.73 (59.17)	72.72 (31.51)
		Stimulation at the control sites					
Vertex	Before stimulation	442.61 (68.69)	510.97 (86)	68.36 (33.4)	406.63 (50.3)	483.66 (69.79)	77.03 (24.27)
	After stimulation	428.05 (62.66)	489.73 (79.02)	61.68 (32.17)	412.76 (60.43)	487.8 (84.7)	75.03 (30.86)

Note. Standard deviations are in parentheses ( ); Congruency score = reaction time of incongruent trials-reaction time of incongruent trials.

4.2 Results of Study Two

4.2.1 Demographic Data

Eighteen participants (male = 10; mean age = 25.3 years; SD = 4.9 years) were recruited by snowball sampling. All of them fulfilled the inclusion criteria. Four had secondary education while fourteen had undergraduate education. Ten had a full-time job while eight were students. Table 4.2a (p. 70) summarises the demographic data of the 18 participants of Study Two. For the score of neuropsychological screening test, the word reading, color naming and incongruent color naming score of Stroop Test were found to 69.81s, 73,65s and 78.52s respectively with mean interference score below 20s. Also, the average self-correction score was below 1. It indicated intact conflict solving ability of rapid-adaptive control function. For the perseverative errors and non-perseverative errors of WCST, the score were 3 and 5.15, respectively that were within the scores 9 and 10. It implied the set-shifting ability of set-maintenance control fulfilled the inclusion criteria. The reaction time of CTT I and CTT II was found to be 40.28s and 52.29s, respectively. It showed the intact selective attention ability of the participants. And for the DST-B, the average score of recorded digit span was 6.69, which fulfilled the working memory criteria of the inclusion. Table 4.2b (p. 71) summarises the neuropsychological screening test results of the participants.

Table 4.2a

Demographics of the 18 participants of Study Two

Male (%)		10 (55.6)
Age (SD) (years)		25.3 (4.9)
Educational Level (%)		
	Secondary	4 (22.2)
	Undergraduate	14 (77.8)
Employment state (%)		
	Full-time	10 (55.6)
	Student	8 (44.4)

Note. SD = standard deviations.

Table 4.2b

Test scores of the screening neuropsychological tests of the participants of Study Two

Stroop Test	
Word Reading	
Total Time (second)	69.81 (12.83)
Self-correction	0.23 (0.44)
Color Naming	
Total Time (second)	73.65 (13.12)
Self-correction	0.31 (0.48)
Incongruent Color Naming	
Total Time (second)	78.52 (11.54)
Self-correction	0.54 (0.66)
Difference Score	
IN – WR (second	12.03 (9.84)
IN – CN (second)	15.63 (11.2)
Wisconsin Card Sorting Test	
Perseverative errors	3 (0.82)
Non-perseverative errors	5.15 (1.46)
Color Trails Test	
Color Trails Test-I (second)	40.28 (8.73)
Color Trails Test-II (second)	52.29 (6.55)
Digit Span Test- Backward	
Digit span	6.69 (0.48)

Note. Standard deviations are in parentheses ( )

4.2.2 Behavioural Results

Study Two aimed to investigate how the iTBS-induced activation of the substrates of the dual top-down networks (i.e., the CON: aI/fO, dACC/msFC, and aPFC; FPN: dlPFC and dFC) may differentially influence the subsequent performance of the Flanker task, in terms of reaction time, under higher and lower demands of set-maintenance, and rapid-adaptive executive control.

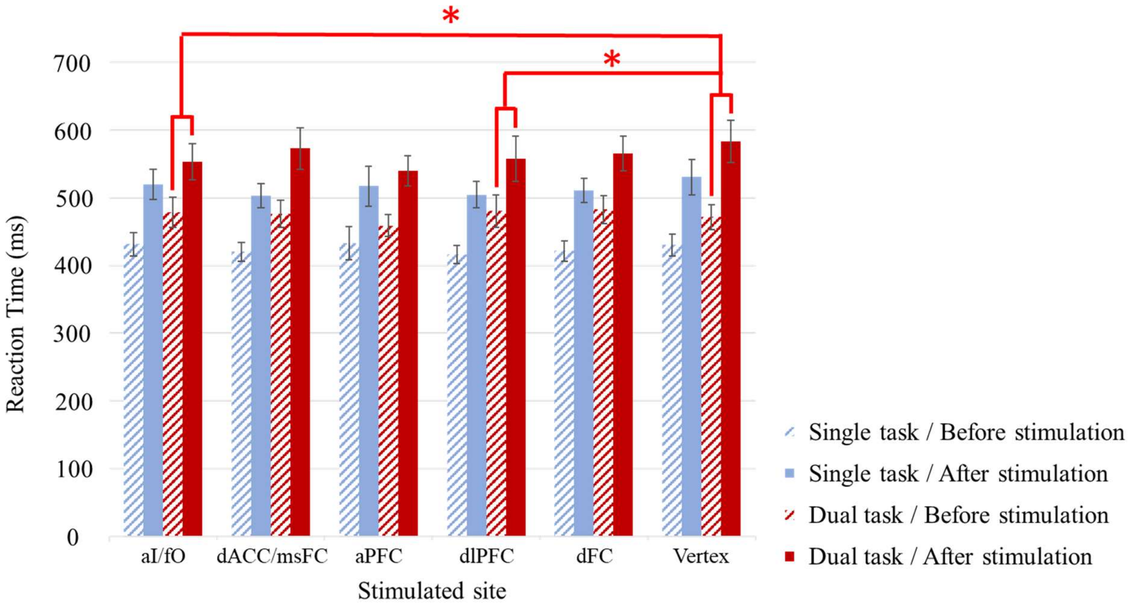
Three-way repeated measures ANOVA model of task conditions (single- and dual-task conditions) × congruency (congruent and incongruent trials) × stimulation sites (the CON: aI/fO, dACC/msFC, and aPFC; the FPN: dlPFC and dFC; control: the vertex) revealed significant interaction stimulation effect × set-maintenance effect × stimulation sites interaction ($F_{5,85} = 2.96$, $p = 0.016$). To examine the interaction effect, the full model was separated into five ANOVA models in order to compare the reaction time after stimulating at each targeted stimulation site whilst stimulating at the control vertex. Hence, three-way repeated measures ANOVA models of task conditions (single- and dual-task conditions) × congruency (congruent and incongruent trials) × stimulation sites targeted stimulation sites and vertex) were conducted for the five stimulation sites (the CON: aI/fO, dACC/msFC, and aPFC; the FPN: dlPFC and dFC). The significant interaction effect of the task conditions × congruency × stimulation sites was found only in the model of aI/fO ($F_{1,17} = 7.38$, $p = 0.015$) and dlPFC ($F_{1,17} = 8.90$, $p =$

0.008) but not in the other sites ($p > 0.05$). For the iTBS stimulation at the aI/fO site, post-hoc tests of 2-way repeated measures ANOVA revealed significant interaction effect of congruency (congruent and incongruent trials) × stimulation sites (aI/fO and the vertex) in the dual-task condition ($F_{1,17} = 10.42$, $p = 0.005$, see Figure 4.2a, p. 74) but not in the single-task condition ($F_{1,17} = 0.76$, $p = 0.395$). The interaction effect of congruency × stimulation sites (aI/fO and the vertex) in the dual-task condition showed shorter reaction time when performing the incongruent trials after stimulating at aI/fO ($M = 553.36$s, $SD = 114.09$s) compared with stimulating at the vertex ($M = 583.26$s, $SD = 131.85$s) but not in the reaction time when performing the congruent trials (aI/fO: $M = 478.85$s, $SD = 92.84$s; vertex: $M = 471.85$s, $SD = 78.88$s). For the iTBS stimulation applied at the dlPFC sites, post-hoc tests of 2-way repeated measures ANOVA revealed significant interaction effect of congruency (congruent and incongruent trials) × stimulation sites (dlPFC and the vertex) in the dual-task condition ($F_{1,17} = 12.46$, $p = 0.003$, see Figure 4.2a, p. 74) but not in the single-task condition ($F_{1,17} = 2.21$, $p = 0.155$). The interaction effect of congruency × stimulation sites (dlPFC and vertex) in the dual-task condition showed significantly shorter reaction time when performing incongruent trials after iTBS stimulations at dlPFC ($M = 557.99$s, $SD = 142.87$s) compared with the iTBS stimulations at the vertex ($M = 583.26$s, $SD = 131.85$s) but no significant interaction effects were found when performing the congruent trials (dlPFC: $M = 480.47$s, $SD = 102.83$s; vertex:

M = 471.85s, *SD* = 78.88s). Table 4.2c (p. 75) shows the mean reaction time of the Flanker task in different task conditions (dual-task and single-task) and congruency trials (congruent and incongruent) effect after stimulating at the six selected cortical sites, i.e., three CON sites, aI/fO, dACC/msFC and aPFC, two FPN sites, dlPFC and dFC, and the vertex (the control site).

Figure 4.2a

The Reaction Time of Flanker Task across Stimulated Sites in Study Two



Note. * < 0.01, total number *N* = 18, the error bars represent the standard error of the mean

Table 4.2c

Reaction time (mean and standard deviations) in tasks with different conditions (dual-task and single-task conditions) and congruency (congruent and incongruent trials) after stimulating at the six different cortical sites, i.e., aI/fO, dACC/msFC, aPFC, dlPFC, dFC, and the vertex

	Dual-task condition (ms)		Single-task condition (ms)	
	Congruent trials	Incongruent trials	Congruent trials	Incongruent trials
Stimulation at the CON sites				
aI/fO	478.85 (92.84)	553.36 (114.09)	431.47 (72.68)	519.99 (94.3)
dACC/msFC	476.17 (85.19)	573.31 (130.44)	420.35 (60.13)	503.1 (76.24)
aPFC	459.18 (66.9)	539.64 (94.12)	433.12 (104.43)	517.54 (125.27)
Stimulation at the FPN sites				
dlPFC	480.47 (102.83)	557.99 (142.87)	416.3 (55.45)	504.56 (82.58)
dFC	482.82 (86.96)	566.02 (107.94)	421.55 (65.26)	511.34 (76.66)
Stimulation at the control sites				
Vertex	471.85 (78.88)	583.26 (131.85)	430.73 (68.9)	530.6 (108.97)

Note. Standard deviations are in parentheses ( ).

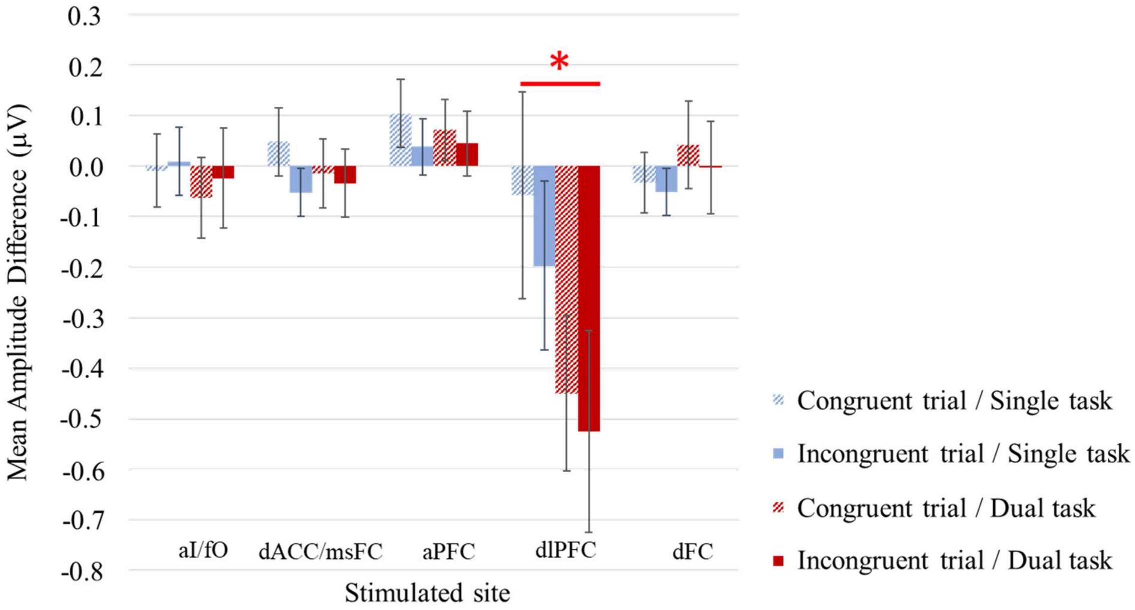
4.2.3 ERP, TFA and Effective Connectivity Results

4.2.3.1 Amplitude of the Stimulus-Preceding Negativity (SPN) Component for Task-Set Implementation.

To explore how the activation of dual network substrates may have influenced the neural process of task-set implementation, a three-way ANOVA model of task conditions (single- and dual-task conditions) × congruency (congruent and incongruent trials) × stimulation sites (the CON: aI/fO, dACC/msFC, and aPFC; the FPN: dlPFC and dFC) revealed significant interaction effect task conditions × stimulation sites ($F_{4,68} = 4.99$, $p = 0.001$) at the Fz sites. For each of the stimulation sites (i.e., aI/fO, dACC/msFC, aPFC, dlPFC, and dFC), post-hoc tests of two-way ANOVA model of task conditions (single- and dual-task conditions) × congruency (congruent and incongruent trials) was conducted on the amplitude differences. The amplitude of the SPN component was found to be significantly more negative in the dual-task condition ($M = -0.49\mu V$, $SD = 0.75\mu V$) compared with that in the single-task condition ($M = -0.18\mu V$, $SD = 0.79\mu V$) only when the iTBS stimulations were applied to dlPFC ($F_{1,17} = 6.79$, $p = 0.018$, see Figure 4.2b, p. 77) but not in other stimulation sites, i.e., aI/fO, dACC/msFC, aPFC, and dFC ($p > 0.1$). Figure 4.2c (p. 78) shows the grand average of the ERP waveform at the Fz site for the dlPFC and vertex stimulations. The calculated mean amplitude difference of the SPN component is showed in Table 4.2d (p. 79) across different demands of the tasks for all five targeted stimulation sites (i.e., the CON: aI/fO, dACC/msFC, and aPFC; the FPN: dlPFC and dFC).

Figure 4.2b

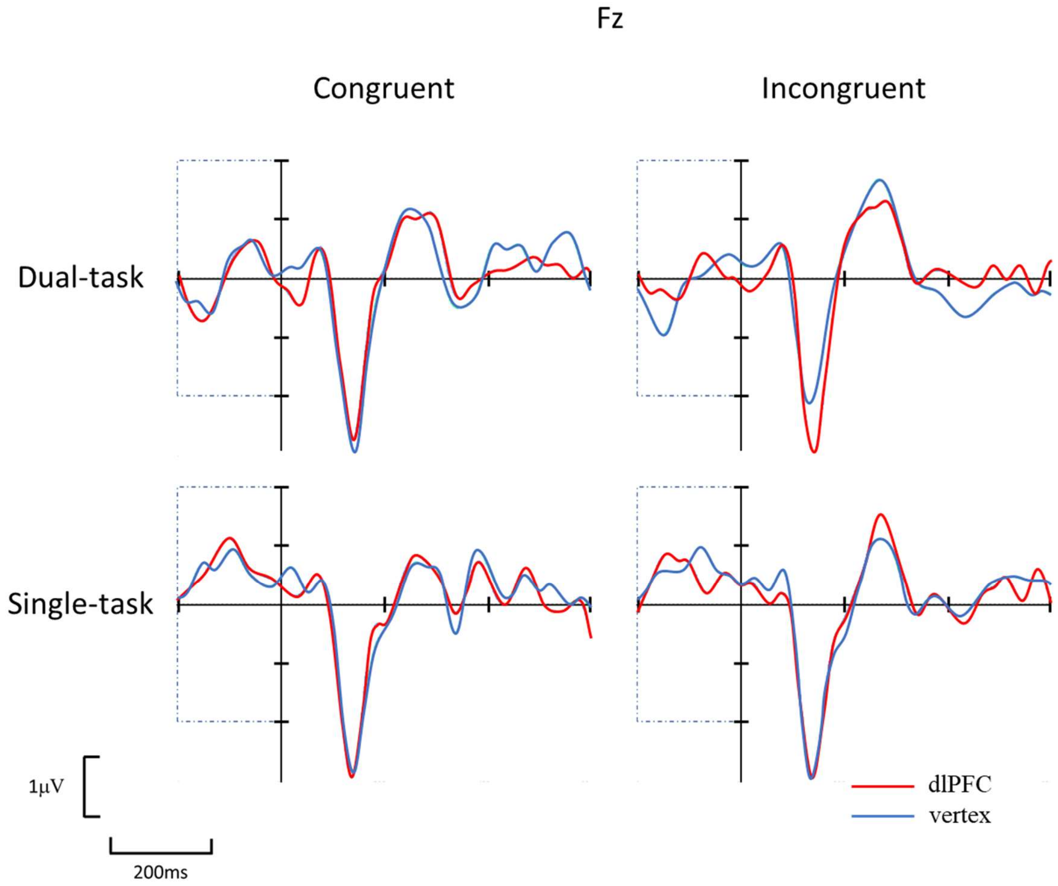
The Mean Amplitude Differences of the SPN Component across Stimulated Sites



Note. * < 0.05, total number $N = 18$, the error bars represent the standard error of the mean

Figure 4.2c

Grand Average ERP Waveform at Fz Recorded during the Flanker Task across Task Condition (Dual- and Single-task Condition) and Congruency Effect (Congruent and Incongruent trials) after Stimulating at dlPFC and Vertex, Showing the SPN Component



Note. The dotted box highlights the SPN component from -200ms to 0ms of target onset.

Table 4.2d

Target-minus-control amplitude differences (mean and standard deviations) of the SPN component in tasks with different conditions (dual-task and single-task conditions) and congruency (congruent and incongruent trials) after stimulating at the five different cortical sites, i.e., aI/fO, dACC/msFC, aPFC, dlPFC, and dFC at the Fz electode site

	Dual-task condition (μV)		Single-task condition (μV)	
	Congruent trials	Incongruent trials	Congruent trials	Incongruent trials
Stimulation at the CON sites				
aI/fO	-0.063 (0.34)	-0.024 (0.421)	-0.009 (0.308)	0.01 (0.286)
dACC/msFC	-0.014 (0.29)	-0.034 (0.286)	0.049 (0.286)	-0.052 (0.202)
aPFC	0.072 (0.259)	0.045 (0.273)	0.105 (0.287)	0.039 (0.238)
Stimulation at the FPN sites				
dlPFC	-0.45 (0.654)	-0.526 (0.847)	-0.057 (0.871)	-0.197 (0.71)
dFC	0.042 (0.366)	-0.003 (0.387)	-0.033 (0.256)	-0.051 (0.199)

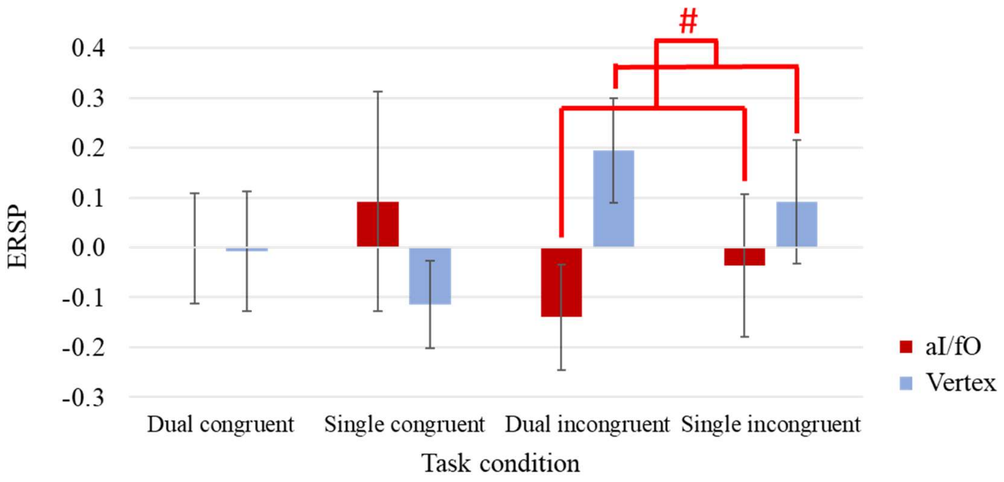
Note. Standard deviations are in parentheses ( ).

4.2.3.2 TFA during Task-set Implementation.

Before analysing the changes of the effective connectivity, the timing of the theta- and alpha-band oscillations were first verified through the method of TFA. The ERSP at Fz electrode site was obtained and compared across four task demands between the iTBS stimulation at each target stimulation site (the CON: aI/fO, dACC/msFC, and aPFC; the FPN: dlPFC and dFC) and stimulation at the vertex. During task-implementation (-200ms – 0 ms), the significant interaction was found in both theta-band and alpha-band oscillations after simulating at the aI/fO compared with the vertex. For the theta-band oscillation, a significant interaction was found between congruency and stimulation sites ($F_{1,17} = 5.082$, $p = 0.038$). The post-hoc tests of two-way repeated measures ANOVA revealed that the ERSP was marginally lower in only incongruent trials after stimulating aI/fO compared with the vertex ($F_{1,17} = 3.113$, $p = 0.096$, see Figure 4.2d, p. 81). For the alpha-band oscillation, a significant interaction effect was found between the factors of congruency and stimulation sites ($F_{1,17} = 4.573$, $p = 0.047$). The post-hoc tests of two-way repeated measures ANOVA revealed that the ERSP was significantly lower in only incongruent trials after stimulating aI/fO compared with the vertex ($F_{1,17} = 4.965$, $p = 0.04$, see Figure 4.2e, p.81). The calculated mean ERSP during task implementation period is showed in Table 4.2e (p. 82) across different demands of the tasks for six stimulation sites (i.e., the CON: aI/fO, dACC/msFC, and aPFC; the FPN: dlPFC and dFC; control: vertex). The mean ERSP of incongruent trial of dual-task condition after stimulating aI/fO and the vertex, and dlPFC and the vertex is plotted in Figure 4.2f (p. 83) and 4.2g (p. 83) respectively. The TFA showed that the theta-band and alpha-band oscillations were influenced by the stimulation of targeted sites during task-set implementation period.

Figure 4.2d

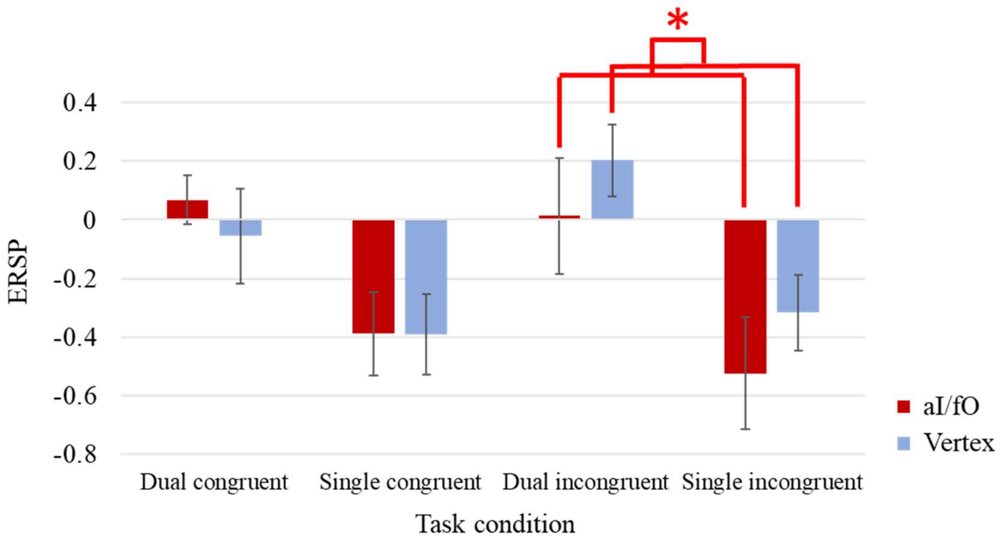
The Mean ERSP of the Theta-Band Oscillation across Four Task Conditions after Stimulating aI/fO and the Vertex at Fz Electrode Site during Task-Set Implementation Period



Note. # < 0.1, total number *N* = 18, the error bars represent the standard error of the mean

Figure 4.2e

The Mean ERSP of the Alpha-Band Oscillation across Four Task Conditions after Stimulating aI/fO and the Vertex at Fz Electrode Site during Task-Set Implementation Period



Note. * < 0.05, total number *N* = 18, the error bars represent the standard error of the mean

Table 4.2e

The ERSP (mean and standard deviations) during task-set implementation period in tasks with different conditions (dual-task and single-task conditions) and congruency (congruent and incongruent trials) after stimulating at the six different cortical sites, i.e., aI/fO, dACC/msFC, aPFC, dlPFC, dFC, and the vertex at Fz electrode site

Oscillation band	stimulation site	Dual-task condition		Single-task condition	
		congruent	incongruent	congruent	incongruent
	Stimulation at the CON sites				
Theta	aI/fO	-0.002(0.468)	-0.14(0.932)	0.092(0.446)	-0.036(0.604)
	dACC/msFC	-0.121(0.407)	-0.007(0.368)	-0.105(0.336)	-0.226(0.542)
	aPFC	0.241(0.844)	-0.08(0.544)	-0.026(0.328)	-0.227(1.466)
	Stimulation at the CON sites				
	dlPFC	-0.473(1.357)	-0.025(0.436)	-0.171(0.7)	-0.281(0.855)
	dFC	-0.076(0.423)	0.197(0.57)	0.038(0.456)	-0.082(0.494)
	Stimulation at the control site				
	Vertex	-0.007(0.51)	0.195(0.373)	-0.114(0.444)	0.091(0.525)
	Stimulation at the CON sites				
Alpha	aI/fO	0.067(0.354)	0.013(0.603)	-0.388(0.841)	-0.523(0.807)
	dACC/msFC	0.299(0.586)	0.055(0.497)	-0.473(1.003)	-0.561(0.698)
	aPFC	-0.004(0.476)	-0.012(0.486)	-0.38(0.546)	-0.504(0.594)
	Stimulation at the CON sites				
	dlPFC	-0.244(0.671)	-0.012(0.538)	-0.379(0.622)	-0.51(0.648)
	dFC	-0.013(0.678)	0.103(0.611)	-0.464(0.61)	-0.34(0.704)
	Stimulation at the control site				
	Vertex	-0.055(0.684)	0.203(0.581)	-0.39(0.519)	-0.317(0.551)

Note. Standard deviations are in parentheses ( ).

Figure 4.2f

The Mean ERSP Plots of Incongruent Trials after Stimulating a) the Vertex and b) aI/fO at Fz Electrode Site, and c) the t-test Comparison between the Mean ERSP of Two Sites

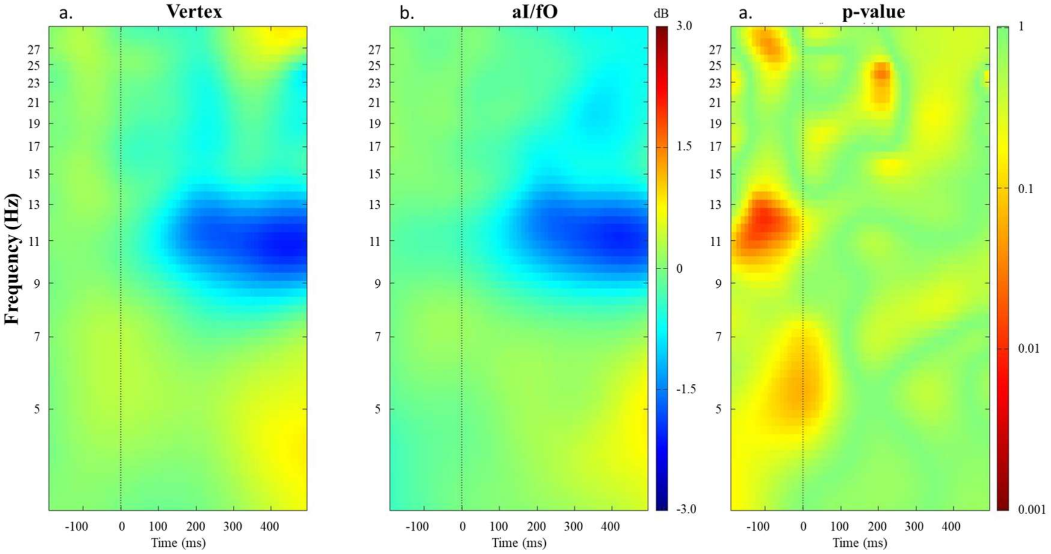
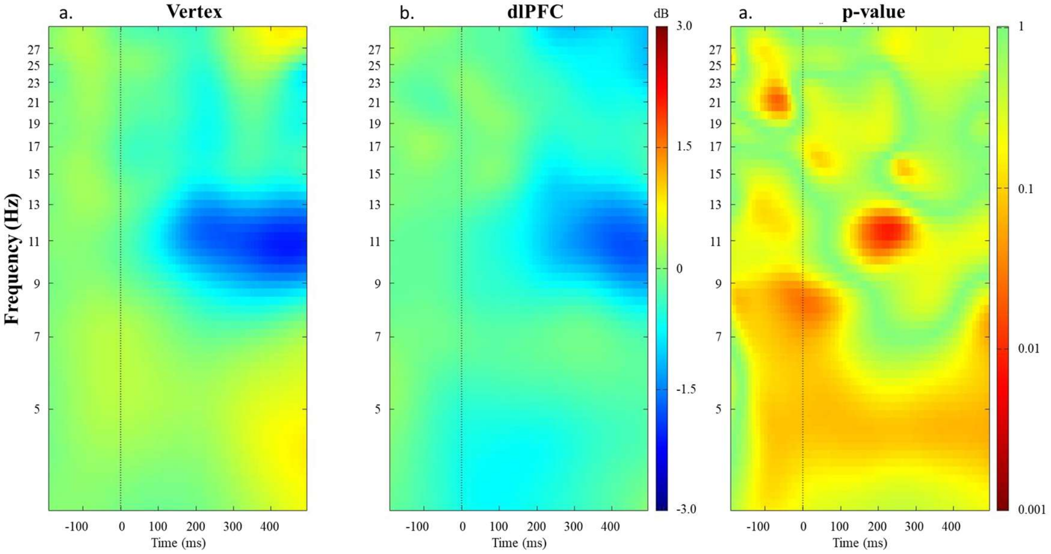


Figure 4.2g

The Mean ERSP Plots of Incongruent Trials after Stimulating a) the Vertex and b) dlPFC at Fz Electrode Site, and c) the t-test Comparison between the Mean ERSP of Two Sites

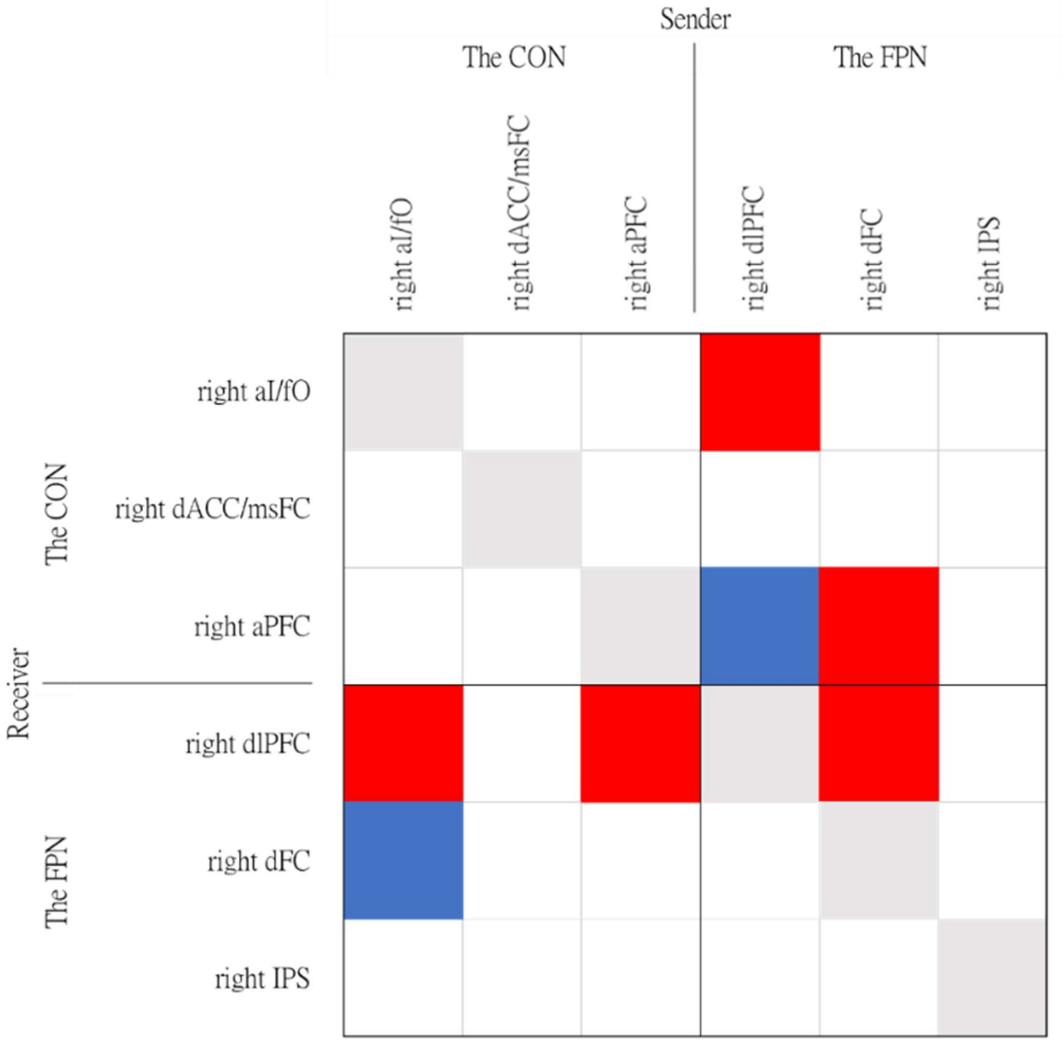


4.2.3.3 Effective Connectivity during Task-set Implementation.

To further investigate how the effective connectivity changed during task-set implementation, statistical comparisons between the stimulation at each stimulation site (the CON: aI/fO, dACC/msFC, and aPFC; the FPN: dlPFC and dFC) and stimulation at the vertex were conducted with the theta-band and alpha-band oscillations separately among the four demand conditions from -200 to 0ms of the target onset, which was the time window confirmed by the TFA. There was significant change found in effective connectivity of the theta-band oscillation under the incongruent trials of the dual-task condition after stimulating at aI/fO with contrasting that at the vertex ($t_{0.1} = 3.99$, $p = 0.005$). The result is showed in Figures 4.2h (p. 85) and 4.2i (p. 86). The red boxes represent the statistically significant increased connectivity flows of oscillation found in the condition after stimulating at aI/fO compared with after stimulating at the vertex. The blue boxes represent the opposite result of the decreased connectivity flows of oscillation found after the iTBS stimulation at aI/fO. Under the incongruent trials of the dual-task condition, the increased flow of the theta-band oscillation was found from aI/fO to dlPFC, and from dlPFC to aI/fO. Such that increased bidirectional flows were found between the key substrate of the CON and FPN. Besides, two increased connectivity were found across dual networks, including from aPFC to dlPFC, and from dfC to aPFC. The decrease information flows of the theta oscillation were found from dlPFC to aPFC, and from aI/fO to dFC.

Figure 4.2h

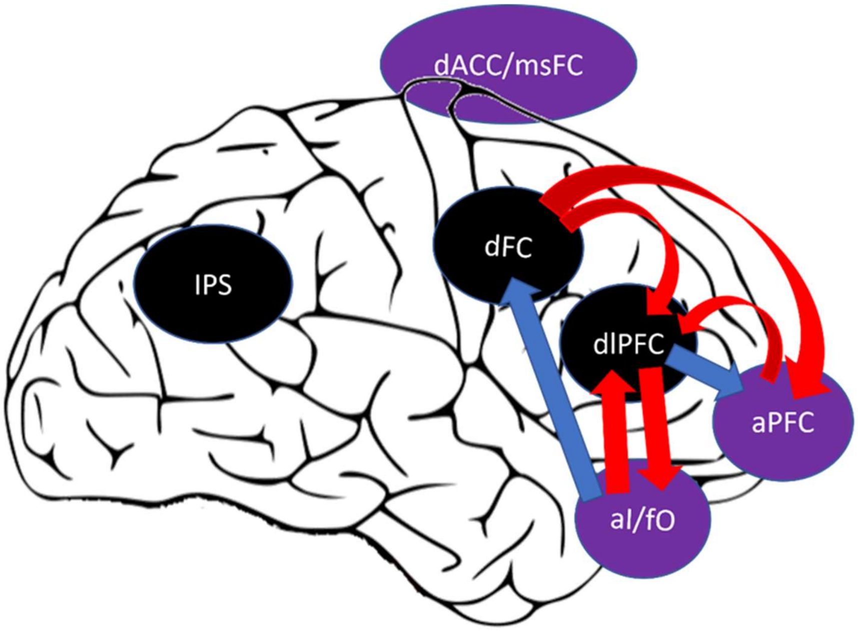
Results of Changes of ICoh in the Theta-band Oscillation after Stimulating at aI/fO under Incongruent Trials of Dual-task Condition during Task-set Implementation



Note. Significant changes of effective connectivity in the theta-band oscillation under the incongruent trials of the dual-task situation after t-statistics comparing stimulating at aI/fO minus stimulating at the vertex. The flow of the theta-band oscillation activity is plotted in matrix fashion; the columns represent "senders" while the rows are "receivers" of information flow. Red squares indicate effective connectivity after stimulating at aI/fO > effective connectivity after stimulating at the vertex; blue squares indicate the opposite change. The colours correspond to $p < 0.05$ (SnPM) at the t-threshold = 3.99.

Figure 4.2i

Results of changes of Effective Connectivity of the Theta-band Oscillation after Stimulating at aI/fO under Incongruent Trials of Dual-task Condition during Task-set Implementation



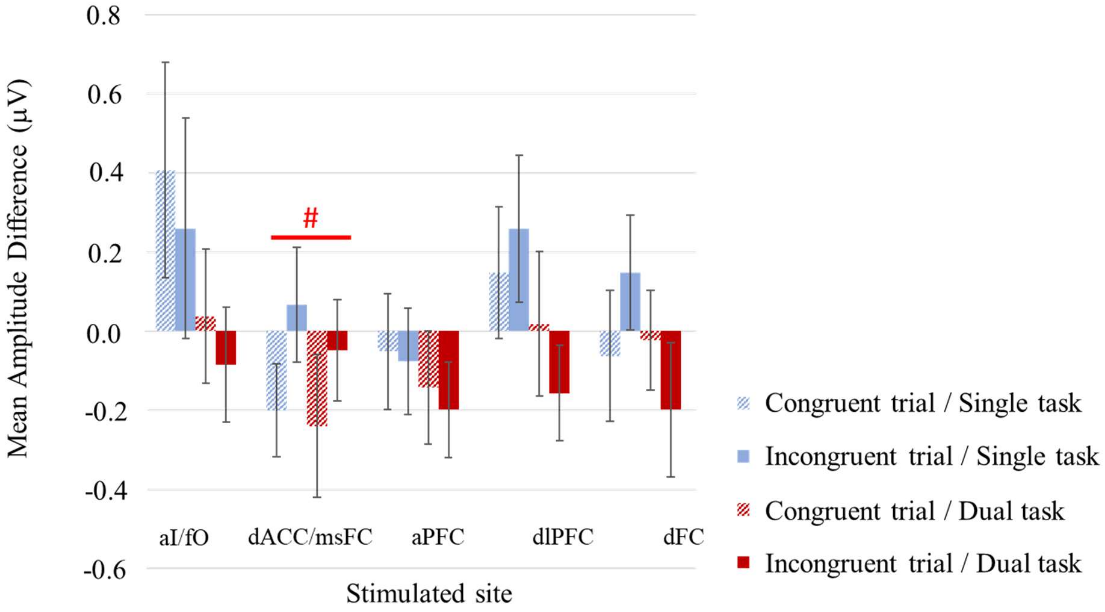
Note. Changes of effective connectivity showed with right lateral views of the inflated brain surface. The red arrows indicate effective connectivity after stimulating at aI/fO > effective connectivity after stimulating at the vertex; blue arrows indicate the opposite change. The purple ovals represent the substrates of the CON; the black ovals represent the substrates of the FPN.

4.2.3.4 Amplitude of the N1 Component for Information Processing.

To explore how the activation of each dual network substrate may have differentially influenced the neural process of information processing, a three-way ANOVA model of task conditions (single- and dual-task conditions) × congruency (congruent and incongruent trials) × stimulation sites (the CON: aI/fO, dACC/msFC and aPFC; the FPN: dlPFC and dFC) on the amplitude differences revealed significant interaction effect congruency × stimulation sites ($F_{4,68} = 2.63$, $p = 0.042$). Post-hoc tests of two-way ANOVA model of task conditions (single- and dual-task conditions) × congruency (congruent and incongruent trials) was conducted on the amplitude differences for each of the stimulation sites (the CON: aI/fO, dACC/msFC, and aPFC; the FPN: dlPFC and dFC). The results showed marginally significant more negative N1 component was found in the congruent trials ($M = -0.22\mu V$, $SD = 0.41\mu V$) compared with the incongruent trials ($M = -0.01\mu V$, $SD = 0.36\mu V$) after stimulating at only dACC/msFC ($F_{1,17} = 3.82$, $p = 0.067$, see Figure 4.2j, p. 88) but not in the other stimulation sites, i.e., aI/fO, aPFC, dlPFC, and dFC ($p > 0.1$). Figure 4.2k (p. 89) shows the grand average of the ERP waveform at the Pz site for the dACC/msFC and vertex stimulation. The calculated mean amplitude difference of the N1 component is shown in Table 4.2f (p. 90) across the different demands of the tasks for all five targeted stimulation sites (i.e., the CON: aI/fO, dACC/msFC, and aPFC; the FPN: dlPFC and dFC).

Figure 4.2j

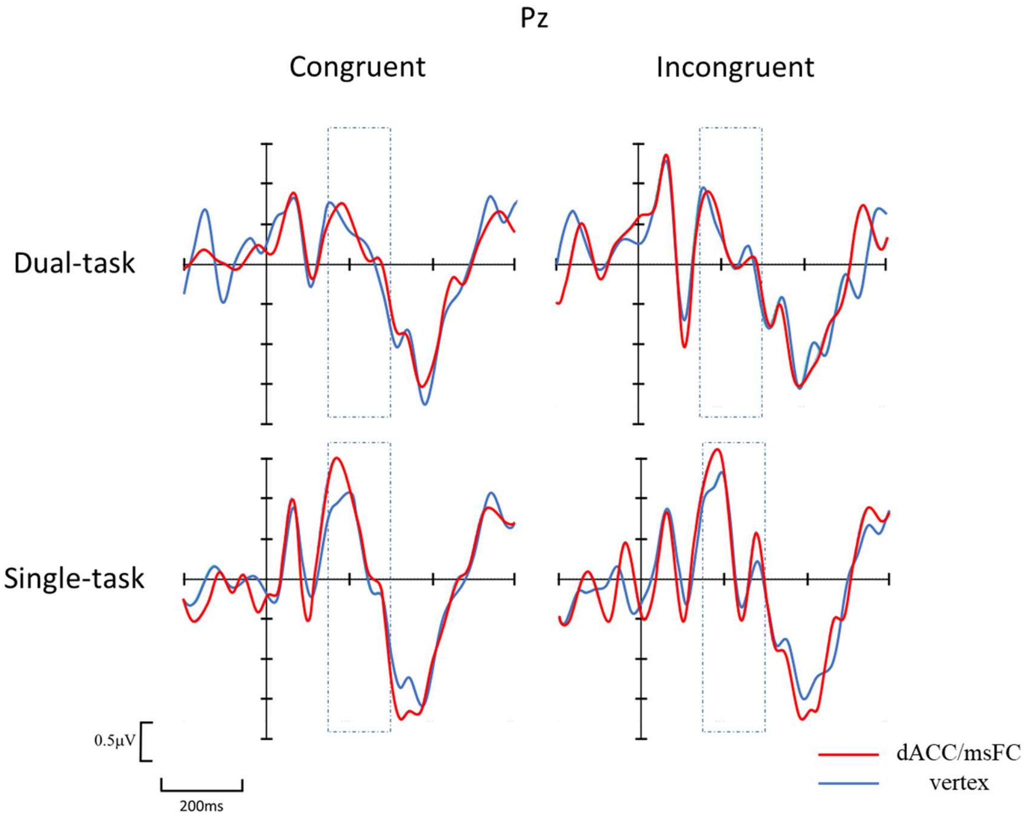
The Mean Amplitude Differences of the N1 Component across Stimulated Sites



Note. # < 0.1, total number *N* = 18, the error bars represent the standard error of the mean

Figure 4.2k

Grand Average ERP Waveform at Pz Recorded during the Flanker Task across Task Condition (Dual- and Single-task Condition) and Congruency Effect (Congruent and Incongruent trials) after Stimulating at dACC/msFC and Vertex, Showing the N1 Component



Note. The dotted box highlights the N1 component from 150ms to 300ms of the target onset.

Table 4.2f

Target-minus-control amplitude differences (mean and standard deviations) of the N1 component in tasks with different conditions (dual-task and single-task conditions) and congruency (congruent and incongruent trials) after stimulating at the five different cortical sites, i.e., aI/fO, dACC/msFC, aPFC, dlPFC, and dFC at the Pz electrode stie

	Dual-task condition (μV)		Single-task condition (μV)	
	Congruent trials	Incongruent trials	Congruent trials	Incongruent trials
Stimulation at the CON sites				
aI/fO	0.038 (0.723)	-0.084 (0.615)	0.407 (1.158)	0.26 (1.185)
dACC/msFC	-0.24 (0.763)	-0.048 (0.543)	-0.2 (0.495)	0.068 (0.615)
aPFC	-0.142 (0.607)	-0.199 (0.508)	-0.051 (0.619)	-0.077 (0.569)
Stimulation at the FPN sites				
dlPFC	0.019 (0.776)	-0.156 (0.511)	0.148 (0.705)	0.26 (0.787)
dFC	-0.023 (0.536)	-0.198 (0.719)	-0.063 (0.701)	0.147 (0.616)

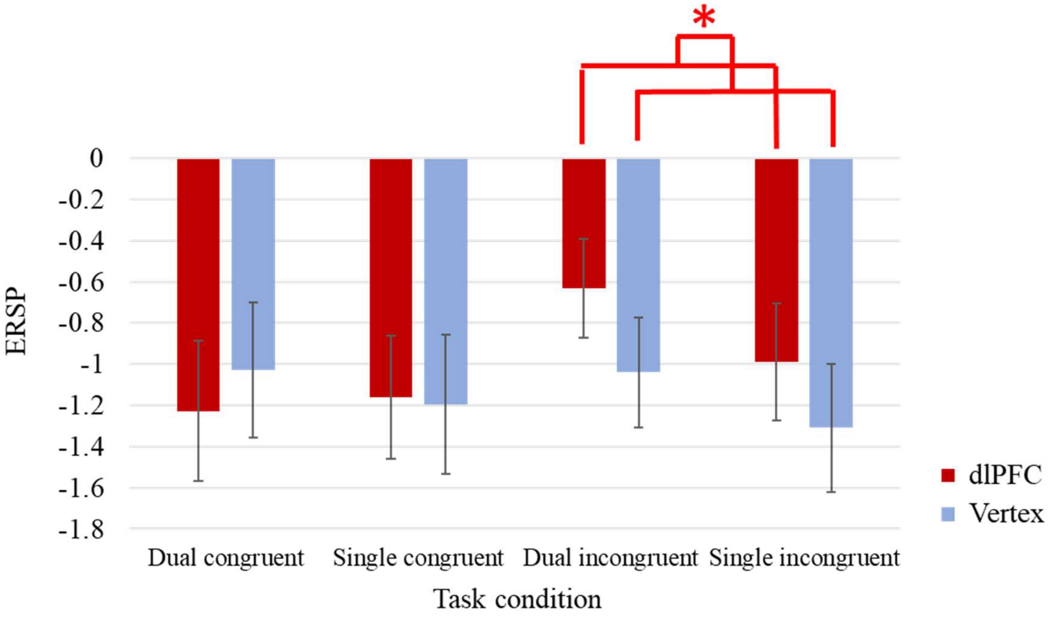
Note. Standard deviations are in parentheses ( ).

4.2.3.5 TFA during Information Processing.

To verify the theta- and alpha-band oscillations during information processing (150ms–300ms), the mean ERSP at Fz electrode site was obtained. The ERSP was compared across four task demands between the stimulation at each target stimulation site (the CON: aI/fO, dACC/msFC, and aPFC; the FPN: dlPFC and dFC) and stimulation at the vertex. During information processing, no significant interaction was found betweem stimulation site while a marginal significant interaction was found in the theta-band oscillation after simulating at the dlPFC compared with the vertex. The marginal interaction was found between congruency and stimulation sites (*$F_{1,17}$* = 4.168, *p* = 0.057). The post-hoc tests of two-way repeated measures ANOVA revealed that the ERSP was significantly higher in only incongruent trials after stimulating dlPFC compared with the vertex (*$F_{1,17}$* = 4.900, *p* = 0.041, see Figure 4.2l, p.92). The calculated mean ERSP during information processing period is showed in Table 4.2g (p. 93) across different demands of the tasks for six stimulation sites (i.e., the CON: aI/fO, dACC/msFC, and aPFC; the FPN: dlPFC and dFC; control: vertex). The mean ERSP of incongruent trial after stimulating dlPFC and the vertex is plotted in Figure 4.2g (p. 83). The TFA results showed that the theta-band oscillation was influenced by the stimulation of targeted sites during information processing period.

Figure 4.2l

The Mean ERSP of the Theta-Band Oscillation across Four Task Conditions after Stimulating dlPFC and the Vertex at Fz Electrode Site during Information Processing Period



Note. * < 0.1, total number *N* = 18, the error bars represent the standard error of the mean

Table 4.2g

The ERSP (mean and standard deviations) during information processing period in tasks with different conditions (dual-task and single-task conditions) and congruency (congruent and incongruent trials) after stimulating at the five different cortical sites, i.e., aI/fO, dACC/msFC, aPFC, dlPFC, dFC, and the vertex at Fz electrode site

Oscillation band	stimulation site	Dual-task condition		Single-task condition	
		congruent	incongruent	congruent	incongruent
	Stimulation at the CON sites				
Theta	aI/fO	0.017(1.124)	-0.008(1.036)	0.681(2.451)	0.151(0.922)
	dACC/msFC	-0.01(0.75)	0.099(0.622)	0.076(0.907)	-0.054(0.807)
	aPFC	-0.25(1.656)	-0.169(0.543)	-0.547(2.813)	0.075(0.915)
	Stimulation at the CON sites				
	dlPFC	-0.437(1.571)	0.073(0.944)	-0.03(0.864)	-0.703(2.227)
	dFC	-0.024(1.031)	0.018(0.867)	-0.033(0.78)	0.05(0.682)
	Stimulation at the control site				
	Vertex	0.085(0.765)	0.14(0.675)	0.058(0.875)	-0.056(0.685)
	Stimulation at the CON sites				
Alpha	aI/fO	-1.107(1.24)	-0.928(1.399)	-0.704(2.882)	-1.243(1.115)
	dACC/msFC	-0.794(1.605)	-0.705(1.515)	-1.25(1.338)	-1.146(1.207)
	aPFC	-1.144(2.14)	-0.634(1.812)	-1.763(2.287)	-1.013(1.171)
	Stimulation at the CON sites				
	dlPFC	-1.228(1.44)	-0.631(1.266)	-1.16(1.015)	-0.989(1.207)
	dFC	-1.103(1.605)	-0.777(1.765)	-1.322(0.991)	-0.922(1.071)
	Stimulation at the control site				
	Vertex	-1.029(1.393)	-1.04(1.43)	-1.194(1.128)	-1.31(1.32)

Note. Standard deviations are in parentheses ( ).

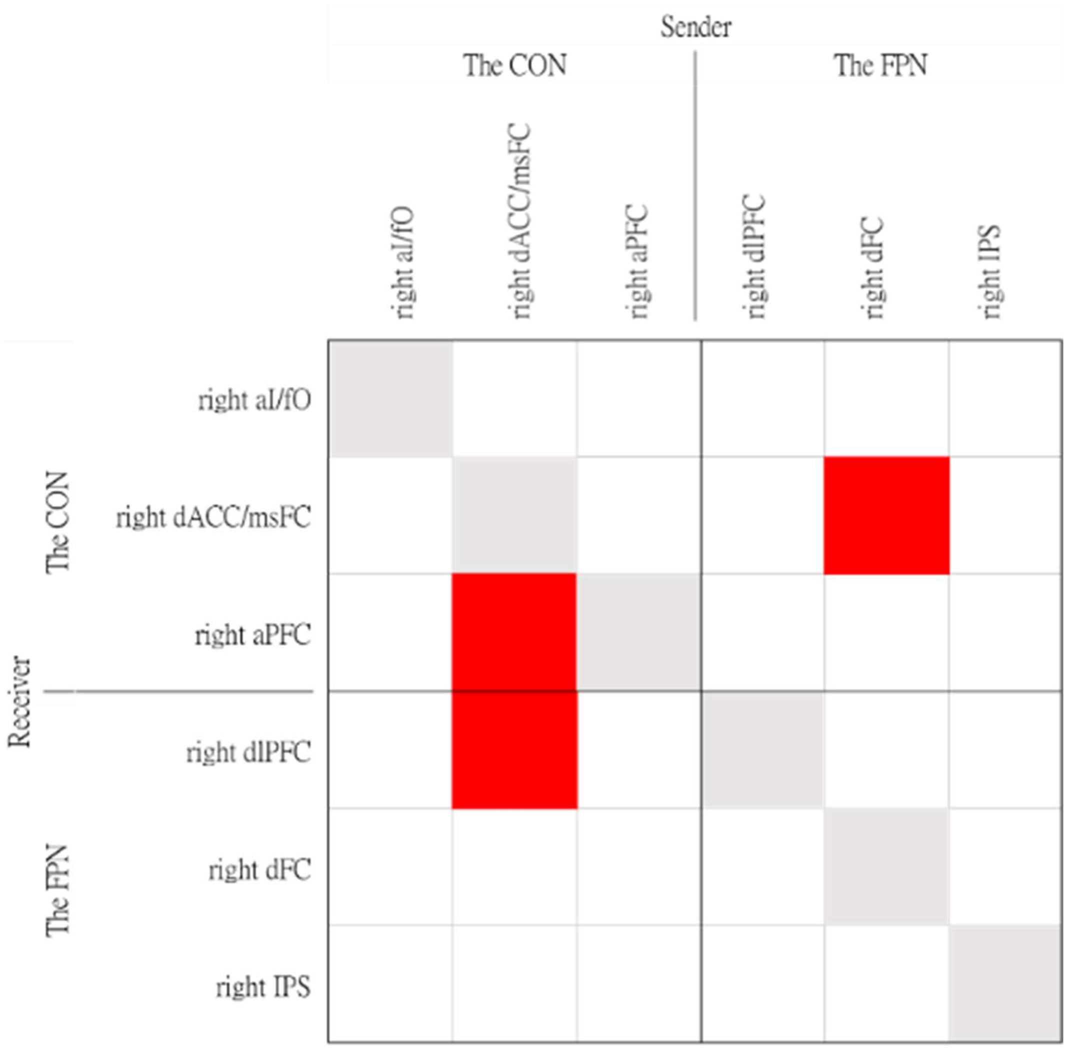
4.2.3.6 Effective Connectivity during Information Processing.

The ICoh analysis was applied on the theta-band and alpha-band oscillations from 150 to 300ms of the target onset, which was the time window confirmed by the TFA, to investigate the differential effect of the neural substrates of the dual networks on changes of effective connectivity during the information processing, Figures 4.2m (p. 96) and 4.2n (p. 97) show the significant changes in connectivity flows of the theta-band oscillation while Figures 10 - 12 show the significant changes in connectivity flows of the alpha-band oscillation. The red boxes represent the statistically significant increased connectivity flows of the oscillation found in the condition after stimulating at the corresponding stimulation site compared with after stimulating at the vertex. The blue boxes represent the opposite result that decreased connectivity flows of the oscillation were found after stimulating at the corresponding stimulation site.

For the theta-band oscillation, the significant changes of effective connectivity were found under the incongruent trials of single-task condition after stimulating at the dlPFC with contrasting that at the vertex ($t_{0.1}$ = 4.30, p = 0.032, see Figures 4.2m and 4.2n p.96 - 97). The result of ICoh revealed that the increased flow of the theta-band oscillation found across the two between network substrates sent from the dFC to the dACC/ msFC and from the dACC/ msFC to and dlPFC. Unexpectedly, the stimulation at dlPFC also increased the flow of the theta-band oscillation from the dACC/ msFC to aPFC, which was connectivity within the CON substrates.

Figure 4.2m

Results of Changes of ICoh in the Theta-band Oscillation after Stimulating at dlPFC under Incongruent Trials of Single-task Condition during Information Processing

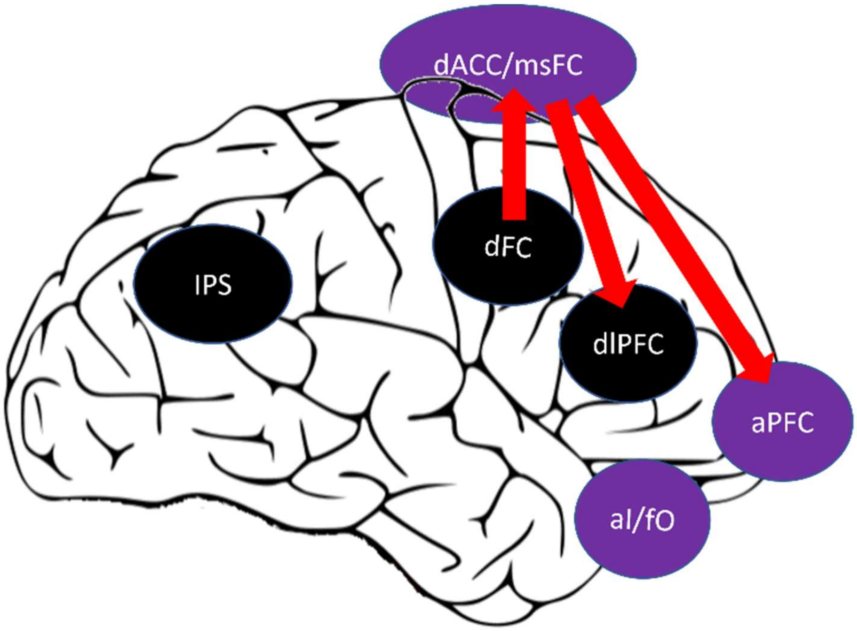


		Sender					
		The CON			The FPN		
Receiver		right aI/fO	right dACC/msFC	right aPFC	right dlPFC	right dFC	right IPS
The CON	right aI/fO	▨					
	right dACC/msFC		▨			🟥	
	right aPFC		🟥	▨			
The FPN	right dlPFC		🟥		▨		
	right dFC					▨	
	right IPS						▨

Note. The flow of the theta-band oscillation activity is plotted in matrix fashion; the columns represent “senders” while the rows are “receivers” of information flow. Red squares indicate effective connectivity after stimulating at the dlPFC > effective connectivity after stimulating at the vertex. The colours correspond to $p < 0.05$ (SnPM) at the t-threshold = 4.3.

Figure 4.2n

Results of Changes of Effective Connectivity in the Theta-band Oscillation after Stimulating at dlPFC under Incongruent Trials of Single-task Condition during Information Processing

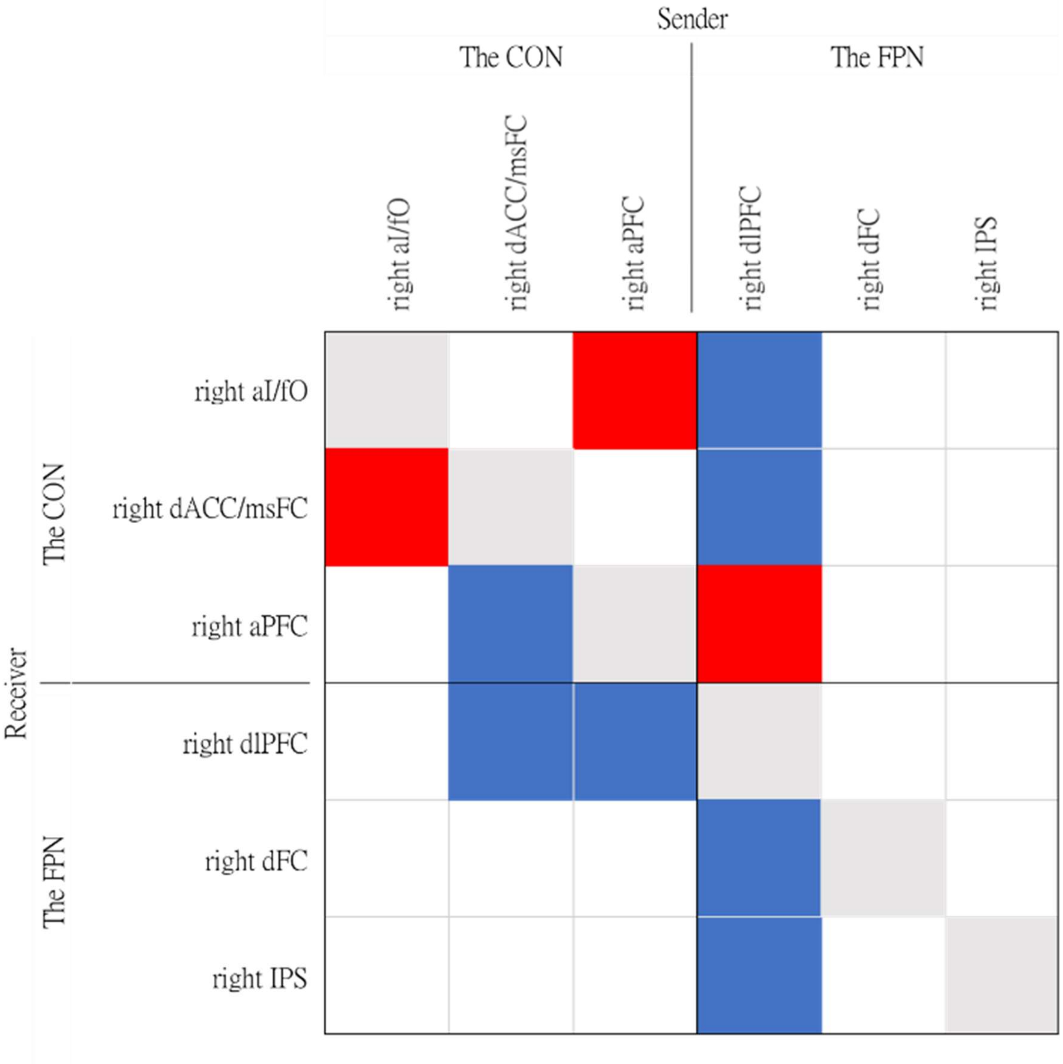


Note. Red arrows indicate effective connectivity after stimulating at the dlPFC > effective connectivity after stimulating at the vertex. The purple ovals represent the substrates of the CON; the black ovals represent the substrates of the FPN.

For the alpha-band oscillation, there were three significant results found in the changes of effective connectivity. All three results of significant changes were under the congruent trials of the dual-task condition stimulating at two substrates of the CON, aI/fO and aPFC, and a substrate of the FPN, dlPFC. For the condition after stimulating at aI/fO, the changes of the alpha-band oscillation flows were relatively complex that included both increased and decreased flows of oscillation sent across within and between network substrates ($t_{0.1} = 4.06$, p = 0.011, see Figures 4.2o and 4.2p, p. 99 - 100). Under the high demand of set-maintenance control, more increased flows of the alpha oscillation were sent within the CON so that the flows sent from aI/fO to dACC/ msFC and also from aPFC to aI/fO. However, the flows of the alpha oscillation decreased from dACC/ msFC to aPFC. Different with the connectivity changes within the CON, mainly decreased oscillation flows of alpha were found in the signals sending to and receiving from the FPN. Only increased alpha oscillation flow was found to be sent from dlPFC to aPFC while two decreased alpha-band oscillation flows were found to be sent from dlPFC to aI/fO and dACC/ msFC. For the changes of flows from the CON to the FPN, connectivity flows of the alpha-band oscillation decreased from both the dACC/ msFC to dlPFC and aPFC to dlPFC. For the change within the FPN network, connectivity flows of the alpha-band oscillation decreased from being sent from dlPFC to dFC and from dlPFC to IPS.

Figure 4.2o

Results of Changes of ICoh in the Alpha-band Oscillation after Stimulating at aI/fO under Congruent Trials of Dual-task Condition during Information Processing

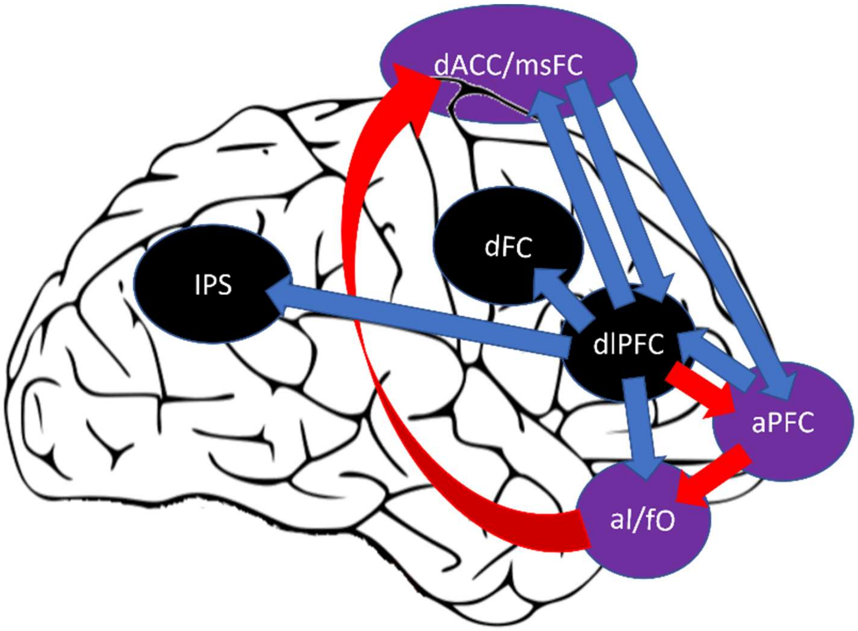


		Sender					
		The CON			The FPN		
		right aI/fO	right dACC/msFC	right aPFC	right dlPFC	right dFC	right IPS
Receiver The CON	right aI/fO	▨		🟥	🟦		
	right dACC/msFC	🟥	▨		🟦		
	right aPFC		🟦	▨	🟥		
The FPN	right dlPFC		🟦	🟦	▨		
	right dFC				🟦	▨	
	right IPS				🟦		▨

Note. The flow of the alpha-band oscillation activity is plotted in matrix fashion; columns represent "senders" while rows are "receivers" of information flow. Red squares indicate effective connectivity after stimulating at aI/fO > effective connectivity after stimulating at vertex; blue squares indicate the opposite change. The colours correspond to $p < 0.05$ (SnPM) at t-threshold = 4.06.

Figure 4.2p

Results of Changes of Effective Connectivity in the Alpha-band Oscillation after Stimulating at aI/fO under Congruent Trials of Dual-task Condition during Information Processing

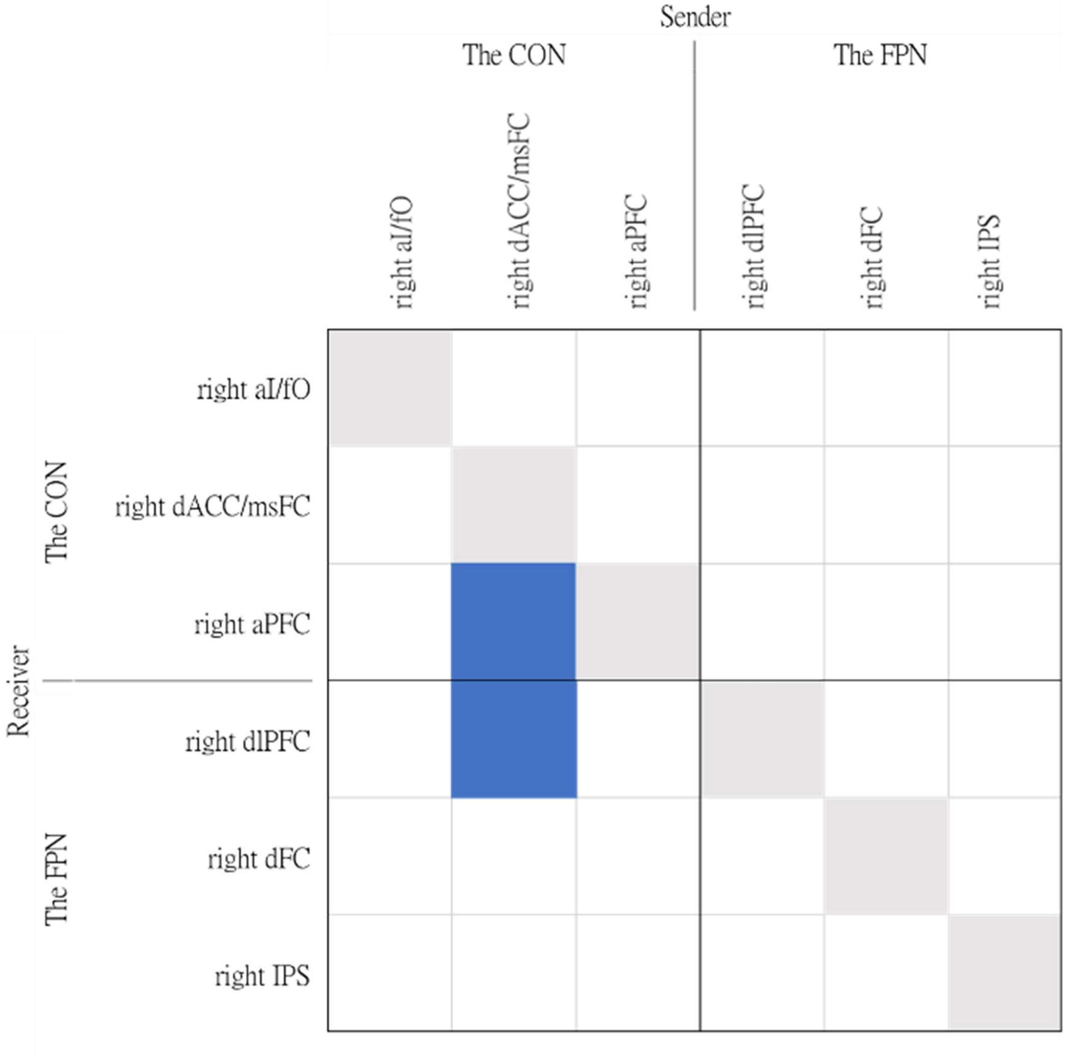


Note. Red arrows indicate effective connectivity after stimulating at aI/fO > effective connectivity after stimulating at vertex; blue arrows indicate the opposite change. The purple ovals represent the substrates of the CON; the black ovals represent the substrates of the FPN.

For the connectivity change found after stimulating at the aPFC, statistical comparisons with vertex stimulation showed only decreased information flows of alpha-band oscillation ($t_{0.1} = 4.23$, $p = 0.026$, see Figures 4.2q and 4.2r, p. 101 - 102). Both of the connectivity changes were found to be sending the flow of the alpha-band oscillation from the CON. The flows of the alpha-band oscillation decreased from dACC/msFC to aPFC and from dACC/msFC to dlPFC. Interestingly, these two decreased flows of oscillations were also found under high set-maintenance demand situation with stimulation at aI/fO.

Figure 4.2q

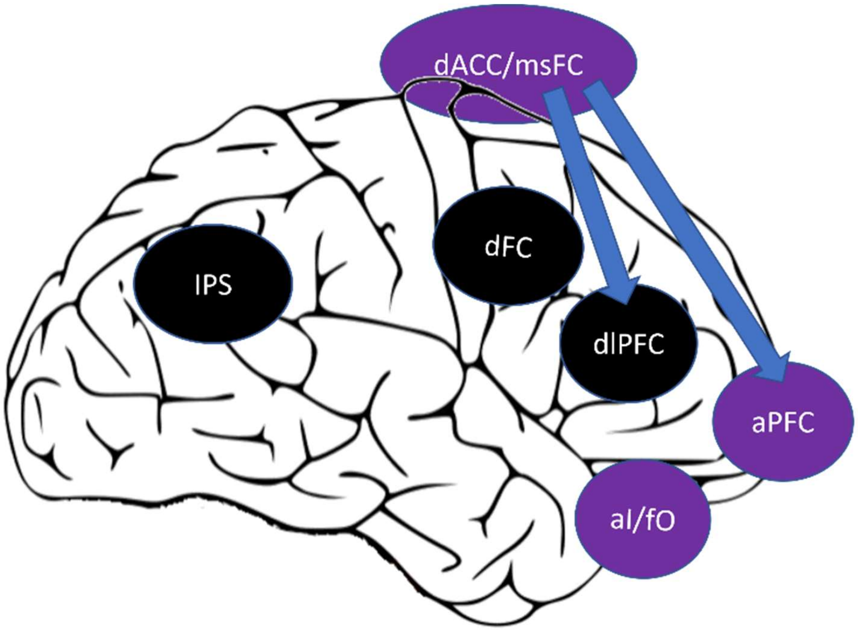
Results of Changes of ICoh in the Alpha-band Oscillation after Stimulating at aPFC under Congruent Trials of Dual-task Condition during Information Processing



Note. The flow of the alpha-band oscillation activity is plotted in matrix fashion; columns represent "senders" while rows are "receivers" of information flow. Blue squares indicate effective connectivity after stimulating at the aPFC < effective connectivity after stimulating at the vertex. The colours correspond to $p < 0.05$ (SnPM) at t-threshold = 4.23

Figure 4.2r

Results of Changes of Effective Connectivity in the Alpha-band Oscillation after Stimulating at aPFC under Congruent Trials of Dual-task Condition during Information Processing

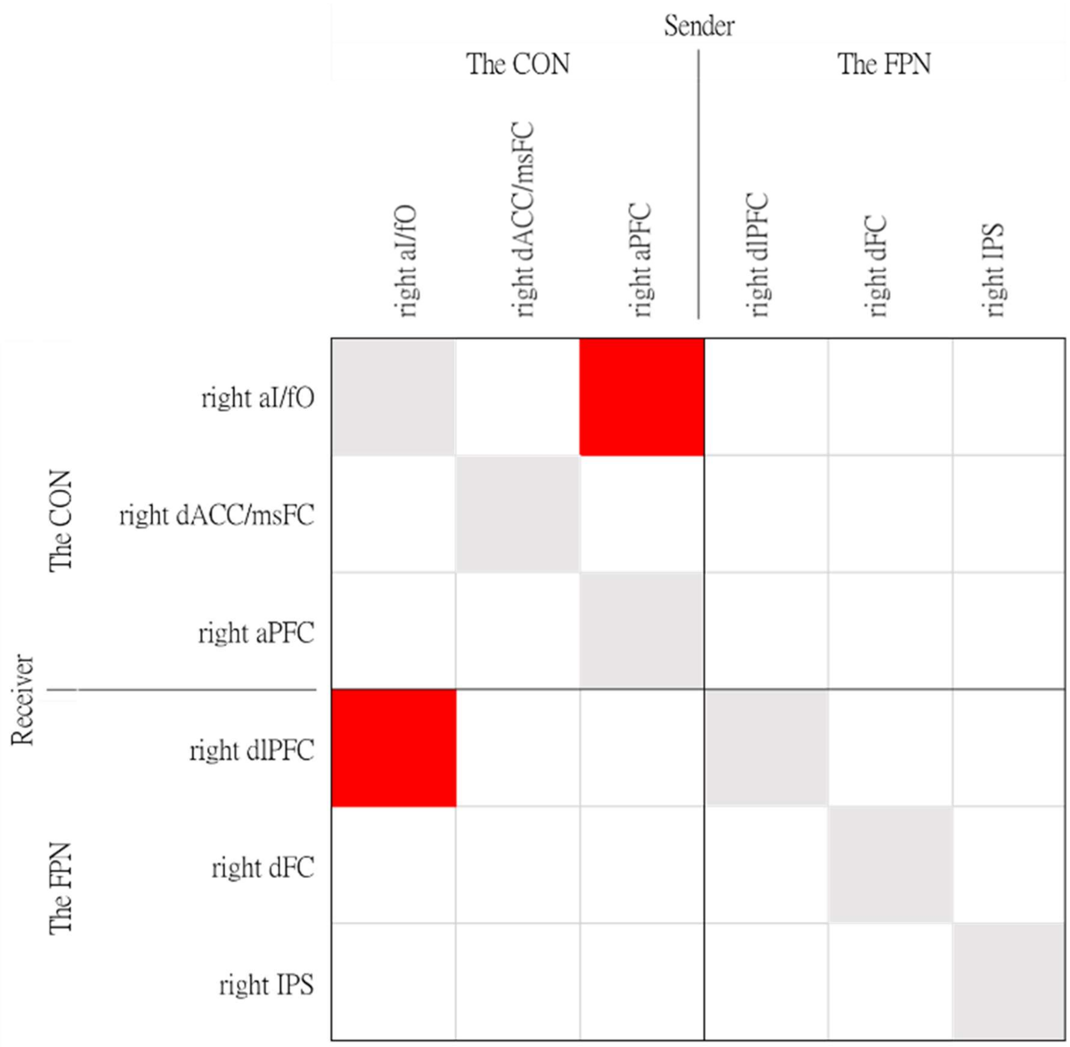


Note. Changes of effective connectivity showed with right lateral views of the inflated brain surface. Blue arrows indicate effective connectivity after stimulating at aPFC < effective connectivity after stimulating at vertex; blue arrows indicate the opposite changes. The purple ovals represent the substrates of the CON; the black ovals represent the substrates of the FPN.

After iTBS stimulating at dlPFC under high set-maintenance demand, statistical comparisons with vertex stimulation showed increased information flow of oscillation ($t_{0.1}$ = 4.28, p = 0.018, see Figures 4.2s and 4.2t, p. 103 - 104). The flow of the alpha-band oscillation was found to increase within the CON that from aPFC to aI/fO, and between network that from aI/fO to dlPFC.

Figure 4.2s

Results of Changes of ICoh in the Alpha-band Oscillation after Stimulating at dlPFC under Congruent Trials of Dual-task Condition during Information Processing

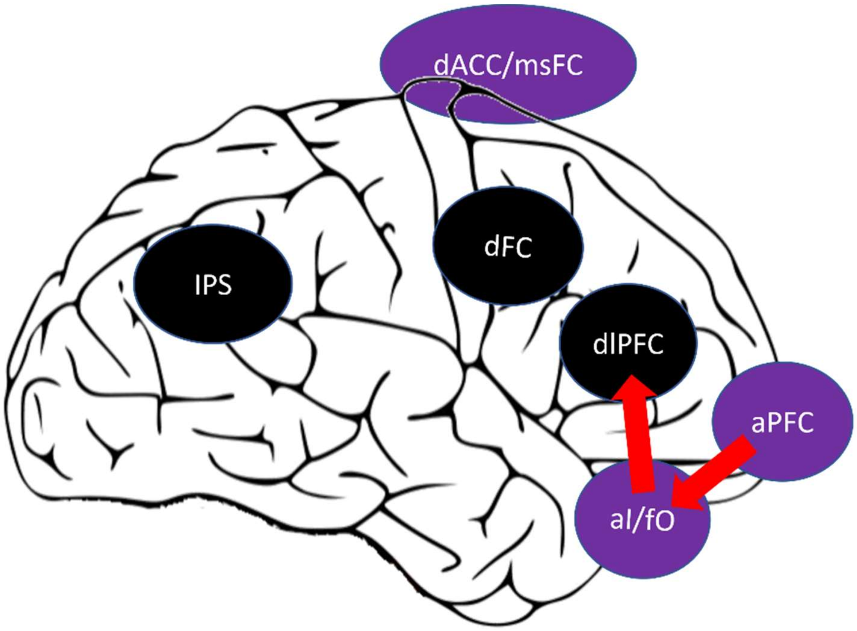


Receiver		Sender					
		The CON			The FPN		
		right aI/fO	right dACC/msFC	right aPFC	right dlPFC	right dFC	right IPS
The CON	right aI/fO	▨		🟥			
	right dACC/msFC		▨				
	right aPFC			▨			
The FPN	right dlPFC	🟥			▨		
	right dFC					▨	
	right IPS						▨

Note. The flow of the alpha-band oscillation activity is plotted in matrix fashion; columns represent “senders” while rows are “receivers” of information flow. Red squares indicate effective connectivity after stimulating at dlPFC > effective connectivity after stimulating at the vertex. The colours correspond to $p < 0.05$ (SnPM) at t-threshold = 4.28.

Figure 4.2t

Results of Changes of Effective Connectivity in the Alpha-band Oscillation after Stimulating at dlPFC under Congruent Trials of Dual-task Condition during Information Processing



Note. Changes of effective connectivity showed with right lateral views of the inflated brain surface. Red arrows indicate effective connectivity after stimulating at dlPFC < effective connectivity after stimulating at vertex. The purple ovals represent the substrates of the CON; the black ovals represent the substrates of the FPN.

CHAPTER FIVE

DISCUSSION

5.1 Discussion of Study One

5.1.1 The Differential Effect of Substrates of the CON under Various Demands on Set-maintenance Control

Study One aimed to investigate the differential effect of activation of the CON substrates, i.e., aI/fO, dACC/msFC and aPFC, on the top-down control performance of a task, indicated by the congruency effect representing the rapid-adaptive function and dual task representing the task-set maintenance function. The results showed, after the iTBS-induced stimulations at aI/fO, the congruency effect was much reduced during the dual-task condition compared with the single-task condition. It was demonstrated that the distinctive role of aI/fO of the CON on modulating the top-down control performance under high set-maintenance demand (i.e., dual-task condition) while this effect on top-down control performance was not shown when the iTBS stimulations were applied on the other substrates of the CON, i.e., dACC/msFC and aPFC. This was consistent to the findings in previous studies (Dosenbach et al., 2006, 2007 & 2008) that aI/fO was one of the core substrates to implement and maintain task-set information across the time course of the task. The current results showed additional information that aI/fO seemed to be more responsible for handling the additional set-maintenance demands in terms of the number of tasksets. Though previous studies also tried to manipulate the demand of set-maintenance with an increasing number of task-sets, they found activation in three of the CON substrates, aI/fO, dACC/msFC, and aPFC (Pillay et al., 2016). This indicated that all three substrates would be involved in order to process extra task-set information. However, the current results found only aI/fO out of three CON substrates may enhance the subsequent performance during the handling of the extra task-set. Different with previous studies, the current study applied the iTBS stimulation to facilitate the activation of the targeted CON substrate. Hence, the processes that may be facilitated by the target stimulation region could be examined. It seemed that the activation of aI/fO may be more influential to alter the effectiveness in order to handle information of the additional task-set, even dACC/msFC and aPFC would also be required to handle the extra demand of the task-set. This may imply that the enhancement of each process alone may not be sufficient to enhance the overall performance.

One of the possible roles of aI/fO may relate to the initiation of connectivity change between the substrates. For example, Kondo et al. (2004) showed that a stronger association between dACC/msFC and dlPFC was required to have better performance in dual-task situation. Interestingly, the current study found that the facilitated activation of dACC/msFC may not lead to better subsequent performance. It implied that the activation of dACC/msFC alone could not directly facilitate its association with dlPFC, but other factors are required. Furthermore, Sheffield et al. (2016) showed that subsequent performance was highly related to the connectivity between the aI/fO and other network substrates. Though Sheffield et al. (2016) used only a number of single tasks in their study, it demonstrated the connections between aI/fO and other substrates may relate to the effectiveness of handling different types of task-set. Unlike msFC/dACC and aPFC, it is speculated that aI/fO may be able to flexibly change the connectivity between other substrates to fulfil the corresponding needs of set-maintenance demands.

5.1.2 The Interaction between the CON and FPN under high demand of Set-maintenance and Rapid-adaptive Control

Besides, the influential effect on set-maintenance demands, it seemed that the aI/fO may also influence the rapid-adaptive performance. The current result found the improved performance only under the incongruent trials of the dual-task situation after stimulating at aI/fO. The targeted arrow in the incongruent trials of the Flanker task should be more difficult to be processed due to the distraction of the inconsistent peripheral arrows, compared with the congruent trials. In another words, the demand of rapid-adaptive control would be higher during the incongruent trials. This indicated that the iTBS-induced activation of aI/fO may facilitate the handling of both set-maintenance and rapid-adaptive demand. The phenomenon is speculated to be accentuated when the timings of the activations are overlapping with each other, i.e., while CON is responsible to handle the two task-sets, the FPN needs to process the incongruent information and maintain the representations in the working-memory buffer. The difference indicated that the facilitation at the aI/fO may not only facilitate the set-maintenance function of the CON but may also facilitate the rapid-adaptive performance of the FPN under higher rapid-adaptive demand.

The previous finding showed that between-network connectivity change was found between the CON and FPN under single-task situation compared with resting-state (Cole et al., 2013; Gordon et al., 2016, 2018). The current findings were consistent with previous studies that the CON and FPN may need to increase connectivity for handling the corresponding demand of task-sets. In addition, the current study may provide two new findings. First, the current study manipulated both the demand of set-maintenance and rapid-adaptive demand and the results showed the interaction was found under higher demand situations. This implied that the interaction between the CON and FPN may be due to task difficulties or demand, which in turn may not be shown by only contrasting task-state with resting-state. With contrasting task-state with resting-state, the changes of between-network connectivity could be due to changing the task needs, such as from visual to auditory system. The current study attempted to induce the changes of network connectivity between the CON and FPN by higher and lower demands of the set-maintenance and rapid-adaptive control. This could mean that the between-network connectivity may not only change for the appropriate types of needs, but also for the appropriate demand of needs. It seemed that stronger between-network connectivity may be needed for higher demand situations. Second, previous studies showed the changes of between-network connectivity between the CON and FPN while the results of the current study suggest that aI/fO may facilitate the changes of the between-network connectivity. At the same time, though the current study showed the aI/fO may also facilitate the rapid-adaptive function of the FPN, the argument about the changes of connectivity may be not strongly supported by behavioural data. Hence, Study Two was subsequently conducted to further investigate how changes of the functional connectivity would be changed due to the higher and lower demands of set-maintenance and rapid-adaptive control. Furthermore, the current study targeted only the CON substrates and showed aI/fO may alter the between-network change. It is yet to be known how the substrates of the FPN may be involved in the changes of connectivity.

5.2 Discussion of Study Two

5.2.1 Both Set-maintenance and Rapid-adaptive Performance Enhanced by aI/fO and dlPFC

The results of Study One demonstrated the iTBS-inducted activation of aI/fO, which is belongs to the CON, may facilitate both set-maintenance and rapid-adaptive performance, which is subserved by the CON and FPN, respectively (Dosenbach et al., 2006, 2007 & 2008) in incongruent trials of the dual-task condition. It implied that the aI/fO of the CON may influence the rapid-adaptive control function, which is subserved by the FPN, under higher set-maintenance and rapid-adaptive demand situation. While increased connectivity between the CON and FPN was revealed when performing a task contrasting with resting state (Cole et al., 2013; Gordon et al., 2018; Gratton et al., 2016), it was yet to be understood how the FPN may have reciprocal influence on in the CON and lead the changes in the related functions. Hence, in Study Two, iTBS were applied to both the CON substrates, i.e., aI/fO, dACC/msFC and aPFC, and the FPN substrates, dlPFC and dFC, to further explore they may differentially influence the set-maintenance and rapid-adaptive performance, in term of behavioural differences and effective connectivity changes. Furthermore, it was also showed that the influential effect of dlPFC of the FPN on subsequence task performance may change across time (Chand & Dhamala, 2017; Kehrer et al., 2015). Study Two, thus, aimed to explore the changes of effective connectivity between the CON and FPN at two selected top-down processes, task-set implementation and information processing.

The results showed that the reaction time of the Flanker task after iTBS stimulations at aI/fO of the CON and dlPFC of FPN became shorter in incongruent trials of dual-task condition compared with that after stimulating at the control site of the vertex. The current results were consistent with that of study one. The iTBS stimulation at aI/fO, compared with the control stimulation, demonstrated the enhancement on the Flanker task performance. A shorter reaction time of the Flanker task was found in incongruent trials of dual-task condition but not in other situations, and this enhancement effect was found in only aI/fO, but not the other substrates of the CON, i.e., dACC/msFC and aPFC. This suggests that the aI/fO among the members of the CON may much influence the both set-maintenance control of the CON and rapid-adaptive control of the FPN.

Apart from the stimulation at aI/fO, the additional finding was that stimulation at dlPFC was similarly enhanced participant's performance in the Flanker task in only incongruent trials of dual-task condition. After iTBS stimulation at dlPFC but not at dFC, a shorter reaction time was found under higher set-maintenance and rapid-adaptive demand, compared with the vertex. First, though with the same network, different substrates of the FPN may differentially influence the set-maintenance and rapid-adaptive performance. Dosenbach et al. (2006) also found difference between the activation of dlPFC in correct trials and incorrect trials across ten different tasks. Previous studies found stronger activation of dlPFC (Pillay et al., 2016) or connectivity between dlPFC and substrates of other networks (Kondo et al., 2004) could under demand of set-maintenance with adding an extra task-set. Compared to other neural substrates of FPN, it is indicated the dlPFC may be more responsible for the varied task demands. The current results further showed that, under iTBS-induced activation, the dlPFC could alter the subsequent set-maintenance and rapid-adaptive performance. Such that dlPFC may not only be activated by the demand of tasks, but it may alter the connectivity change to adopt corresponding needs.

On the hand, the performance of the Flanker task was enhanced only after the iTBS stimulations were applied at aI/fO of the CON and dlPFC of the FPN in incongruent trials of dual-task condition. The aI/fO of the CON and dlPFC of the FPN were expected to be more associated with the set-maintenance control and rapid-adaptive control, respectively (Dosenbach et al., 2006, 2007 & 2008). Both of aI/fO and dlPFC may influence the set-maintenance control and rapid-adaptive control performance indicated that these two substrates may alter the between-network connectivity to handle corresponding cognitive demands. Though aI/fO and dlPFC belongs to two separate networks, they may alter the between-network connectivity similarly during high demand of set-maintenance control and rapid-adaptive control. However, it was unclear their distinct role on the connectivity changes, or otherwise aI/fO and dlPFC may have similar functionality under higher demand of task.

Chand & Dhamala (2017) used EEG methods to measure the cognitive processes in a perceptual decision-making task and revealed that the CON and FPN may influence each other temporally. They based on peak activity of targeted brain region to define two different time windows, from 25 to 225ms, and from 225 to 425ms of stimulus onset. Granger causal analysis was applied on the oscillation activities corresponding to the CON and FPN functions to examine the time course of activations. The results revealed that the CON may have stronger influence on the FPN in 25 - 225ms, while the FPN may have stronger influence on the CON in 225 - 425ms. It indicated that though substrates of both CON and FPN may influence the between-network connectivity, the distinct substrates may have more influence on certain cognitive processes. Different with Chand & Dhamala (2017) that defined specific time-window based on the activity of target substrates, the current study aimed to explore the effect of CON and FPN on selected cognitive processes. Hence, ERP analysis were conducted to examine the differential effect of each network substrate on the task-set implementation and information processing, indicated by the SPN and N1 component respectively. More importantly, ICoh analysis would be used to examine the connectivity change between each network substrate during task-set implementation and information processing. During task-set implementation period, set-maintenance control is expected to implement rules of tasksets. Though dlPFC may also influence set-maintenance function under higher dual-task situation, the CON substrates should have stronger role to handle the task-set. It is speculated that aI/fO of CON may alter the SPN component and the effective connectivity during this period of time. Similarly, the dlPFC may have more influence on the moment-to-moment information process that may alter the N1 component and the effective connectivity during this period of time.

5.2.2 The Differential Effect of the CON and FPN on Task-set Implementation

5.2.2.1 The facilitation of the SPN component by iTBS-induced Activation of dlPFC.

To explore how the activation of the neural substrates of the CON and FPN may differentially influence the task-set implementation under higher and lower level of set-maintenance and rapid-adaptive demand, the SPN component was compared among the iTBS stimulation sites of the CON and FPN. The results revealed a more negative-going SPN component in dual-task condition, compared with in single-task condition, after only stimulating at dlPFC. Previous studies showed a more negative-going SPN component was elicited by higher demand of implementation of upcoming task-sets (Kang et al., 2014; Steinhauser & Steinhauser, 2018). For example, Steinhauser & Steinhauser (2018) manipulated the demand of task-set implementation by the sequence of a dual-task paradigm. The participants need to perform both a Flanker task and a judgement task. The Flanker task was manipulated to one out of two positions, either earlier or later than the judgement task. With comparing these two conditions, the results showed that a more negative-going SPN component was found when the Flanker performed later than the judgement task. It was because the Flanker task-set was needed to immediately implement after the judgement task, which led to a higher demand on set-maintenance control. This demonstrated the more negative-going SPN component would be elicited by the task demand that needed to handle higher set-maintenance demand that maintain an additional task-set during implementation of upcoming event. Different from the analytic approach adopted in previous studies (Kang et al., 2014; Steinhauser & Steinhauser, 2018), the current study demonstrated more negative-going SPN after iTBS was applied at selected sites at the CON (including aI/fO, dACC/msFC, aPFC) and at the FPN (including dlPFC dFC) compared with the iTBS stimulation at the control site (i.e., the vertex). The amplitude difference may signify temporary activation effect of targeted substrates on the SPN component. This indicated the more negative-going SPN found in the current result was due to the influence of the activation dlPFC, but not other activations that were caused by the additional set-maintenance demand. Such that the activation of dlPFC may lead to elicit a more-negative SPN in order to facilitate the handling of an extra task-set during the task-set implementation period. The result was different from the hypothesis that the CON substrates should be more influential on the task-set implementation. One of the possible reasons is that the substrates of the CON, i.e., aI/fO, dACC/msFC, and aPFC, may be highly engaged to maintain additional task-set information while the temporary activation of dlPFC induced by iTBS could provide additional neural resources for preparing upcoming task-set. It may mean that, different from results of the behavioural data that showed enhancement only incongruent trials in the dual-task condition, the iTBS induced activation of dlPFC appeared to influence the SPN component for dual-task condition regardless of the congruency of the trials.

There would be two possibilities to understand the facilitation effect on dlPFC induced by iTBS. First, this facilitation could be due to the changes of interaction between the dlPFC and the substrates of CON. The dlPFC may alter the connectivity of between the CON and FPN during the period of upcoming task-set implementation. Under this situation, the dlPFC would influence the process of the CON. Under this situation, the iTBS-induced activation of dlPFC may provide extra neural resources by increasing the network connectivity between the CON and FPN for the cooperation between two networks. The other possibility would be that this facilitation caused by the only activation of dlPFC itself. It means that the dlPFC may offer additional neural resources to process the extra information of task-set implementation directly. Under this situation, the stronger activation of dlPFC may be found but increased connectivity between the FPN and CON may not be found during the higher demand of set-maintenance control. As discussed, the CON was supposed to be responsible to both implement and sustain the task-set (Dosenbach et al., 2006, 2007 & 2008), and the CON substrates, especially aI/fO, seemed more influential at the earlier period of a task (Chand & Dhamala, 2017). It was speculated that the possibility of the second situation should be higher. Hence, to understand the underlying mechanism of dlPFC on handling additional demand of set-maintenance, the changes of functional connectivity were important to be investigated. Therefore, ICoh analysis was conducted to examine the directional changes of connectivity between the CON and FPN during the task-set implementation period. It was suggested that the aI/fO, but not dlPFC, may alter the connectivity between the CON and FPN and there should be the influence of aI/fO on dlPFC to facilitate the temporary processing of addition al task-set information.

5.2.2.2 The Changes of Effective Connectivity Altered by aI/fO during Task-set implementation.

As the changes of effective connectivity were indicated by the flows of oscillation frequency bands, the iTBS stimulation effect on the oscillation frequency bands of the specific time window was confirmed by the TFA. The TFA results supported that, during the task-set implementation, the iTBS stimulation at aI/fO may decrease the theta- and alpha-band oscillations at frontal region of the brain during higher demand of rapid adative control. The ICoh analysis was conducted to further understand how the flows of oscillations between the substrates of the CON and FPN were changed across the task conditions after iTBS stimulation.

The ICoh results during the timing of the SPN component (-200 – 0ms) showed increased connectivity in the incongruent trials of the dual-task condition during the task implementation period after stimulation had been applied only at aI/fO of the CON. This result matched with the hypothesis that the aI/fO of the CON, compared with dACC/msFC and aPFC, would be highly influential on the changes of connectivity. The current results provided evidence about the effect of the activation of the aI/fO on the change between network connectivity, in terms of reciprocal flow of the theta-band oscillation between aI/fO of the CON to dlPFC of FPN. This indicated that they were required to work with each other under high demand of set-maintenance control and rapid-adaptive control. Also, the iTBS-induced activation of aI/fO may also further enhance the information flow of the theta-band oscillation from aI/fO to dFC of the FPN, and from dlPFC of the FPN to the aPFC of the CON. In contrast to such increased oscillation flow, decreased flow of theta-band was found between other substrates of two networks, that from aI/fO of the CON, and from dlPFC of the FPN to the aPFC of the CON.

There were three observations found in the current results. First, it supported the crucial role of the aI/fO of the CON on modulating task-set implementation compared with other substrates, i.e., dACC/msFC and aPFC. Previous studies demonstrated the increased connectivity between aI/fO and the substrates of other networks may associate with the overall performance of five different tasks while this result did not find in the dACC/msFC and aPFC of the CON (Sheffield et al., 2016). It implied the connectivity changes of the aI/fO may relate to the general ability to handle a number of different task-sets. Furthermore, Gratton et al. (2016) also supported the influential effect of aI/fO with on the changes of connectivity that showed that the activation of aI/fO itself was more related to the changes of between-network and within-network connectivity with contrasting the task-state and resting-state connectivity. They further proposed that there would be some network substrates may alter both between-network and within-network connectivity due to the network structure while the other substrates may not. The current study used iTBS method to induce temporary activation of aI/fO, during specific -200 to 0ms timeframe, to lead the changes of effective connectivity. This result, besides the correlation supports from the task-state fMRI studies, provided additional evidence that aI/fO may actively alter the within- and between-network connectivity to handle task demand related to task-set implementation.

Second, the functional connectivity altered by the activation of the aI/fO may also change the connectivity between the other substrates without direct involvement, for example, increased flow of the theta-band oscillation sent form dFC to aPFC as well as from aPFC to dlPFC. It indicated that the connectivity changes may not only due to the propagation of signal from aI/fO to the other substrates but the activation of aI/fO may also help the CON and the

FPN work together based on their network structure, such that it may alter the overall between-network.

Third, the connectivity changes may be established to meet the specific demand of the task. The changes of connectivity were found included both increased and decreased flow of oscillation for within- and between-network substrates but not an overall increase or decrease of between-network connectivity. It implied these changes of connectivity were not applied to the whole network generally. Cole and his colleagues (2021) demonstrated the specificity of the whole brain between-network connectivity for the task performance. They used the different types of functional connectivity, including resting-state functional connectivity, task-state functional connectivity that averaged across different tasks and also task-state functional connectivity of specific task to predict the subsequent task performance. The results revealed that the functional connectivity of specific task could predict the later performance with higher accuracy than the averaged task-state functional connectivity. And the lowest accuracy of prediction was conducted with the resting-state functional connectivity. It indicated that not only the changes of the connectivity were required for handling the general task demand. These changes of connectivity, though highly similar between each task, would be varied based on the corresponding task demand. Hence, the current study would be important to provide specific change of connectivity between the substrates of the CON and FPN with manipulating the set-maintenance and rapid-adaptive demand.

5.2.2.3 The Distinct Role between aI/fO and dlPFC During Task-set Implementation.

During task-implementation, while the activation of aI/fO of the CON may be more influential to alter the functional connectivity, the activation of dlPFC seemed to be responsible for integrating both task-set and trials initiation information as a helper of aI/fO. Though only the iTBS-induced activation of aI/fO may alter the connectivity, increased flow of the theta-band oscillation found only sent from aI/fO to dlPFC (see Figure 4.2i, p. 86). The most affected substrate was dlPFC that had five changed of effective connectivity found, especially there was both theta-band oscillation sent to and received from aI/fO. It was speculated that aI/fO may mainly alter the between-network connectivity through the help of dlPFC. This suggests that the dlPFC appears to receive increased flow of oscillations from both aPFC of the CON and dFC of the FPN. The aPFC may relate to the planning of complex task-set (Braver et al., 2013; Pillay et al., 2016; Sakai & Passingham, 2003) while the dFC may much relate to the monitoring of trials initiation (Dosenbach et al., 2006, 2007 & 2008). Under high demand of set-maintenance and high rapid-adaptive demand, it seemed the planning of task-set would also require the information of trials initiation so that that plan could carry out timely. The dlPFC might be the substrates for integrating these two pieces of information and then sending feedbacks to the aI/fO. It appears to be consistent with the results of the SPN component that the activation of dlPFC may elicit a more negative-going SPN in dual-task situation. It may be due to dlPFC required additional resources to handle the integration of information sent form aPFC and dFC. And the activated dlPFC did not alter the functional connectivity while the activation of dlPFC may be altered by the activation of aI/fO. It showed the distinct role of aI/fO and dlPFC during the task-set implementation. And this point will be further discussed in general discussion section (see Section 5.3).

5.2.3 The Differential Effect of the CON and FPN on Information Processing

5.2.3.1 The facilitation of the information processing by iTBS-induced Activation of dACC/msFC.

The other key question is how the information processing would be influenced by the activation of the selected neural substrates of the dual networks. The results of the N1 ERP component were found to be marginally less negative in higher information processing demand, i.e., in the incongruent trials, compared with the lower-demand counterpart, i.e., the congruent trials, only after stimulations at the dACC/msFC within the CON but not at other stimulation sites. The current results revealed significantly less negative-going N1 found after iTBS stimulations only at dACC/msFC under high demand of rapid-adaptive, which manipulated by congruent and incongruent trials, regardless the demand of set-maintenance. Similar with the analysis used in the SPN component, the ERP analysis was based on the contrast of the amplitude of N1 components at each of the selected dual network substrates (i.e., the CON: aI/fO, dACC/msFC, aPFC; the FPN: dlPFC dFC) with that of the control site after iTBS stimulations. In contrast, a less negative-going N1 component was elicited by task demand that comparing the dual-task with the single-task condition in previous studies, (Gherri & Eimer, 2010; Little & Woollacott, 2015; Singhal et al., 2002). For example, Gherri and Eimer (2010) demonstrated that, under an additional auditory encoding in dual-task situation, the visual detection task was demanded with sustaining extra encoding task-set. It was suggested that the processing of task relevant information was affected. Compared to the dual-task situation with single visual detection task alone, they find a less negative-going N1. However, these studies contrasted only the single- and dual-task condition but the experimental design did not manipulate the levels of information processing demands. It would be hard to decide whether the N1 reflected the process that handled the extra task-set, or the process that handled the information processing influenced by the extra task-set. And both situations may have required extra cognitive demands to be handled. The results of the current study manipulated both demand of set-maintenance and rapid-adaptive such that these two types of demand could be differentiated from each other. It seemed to support the notion that the reduced negativity of the N1 component may reflect the information processing. Besides, the current study also found this information processing related N1 might be facilitated by the activation of the dACC/msFC which induced by iTBS stimulation. This speculation should be interpreted with caution due to the marginal post-hoc results of the dACC/msFC stimulation ($t_{12} = 2.15$, $p = 0.053$).

Similar to the SPN result of task-set implementation, the analysis result of information processing was also different from the hypothesis that the activation of the FPN substrates may highly influence the rapid-adaptive control performance during the information processing period. The current result showed an opposite trend that dACC/msFC of the CON may have much influence on the information processing under the incongruent trials with the high demand of rapid-adaptive control. It implied that the dACC/msFC of the CON may facilitate processing the trial-related information of rapid-adaptive control, under high demand of task. Under incongruent trials of the Flanker task, which were high demand of rapid-adaptive control, the direction of target arrow was different from the direction of the peripheral arrows. The FPN substrates should be highly engaged to detect the moment-to-moment information to achieve the task-set. The role of dACC/msFC might be to provide additional resource for "highlighting" the task-set, such that FPN substrates could be biased to the target arrow. If this speculation is correct, the connectivity between dACC/msFC and the substrates of FPN is expected to be increased. Kondo et al. (2004) also used a dual-task paradigm with a judgement task and memory task to show the association between the dACC/msFC and dlPFC in good performers compared with poor performers. Though this study used dual-task paradigm that may cause higher demand of task-set, the contrast between the good performers and poor performers may differentiate the ability to process task relevant information during the task. This study showed, in good performers but not poor performers, increased connectivity between dACC/msFC and dlPFC would be required in order to facilitate the information processing under dual-task situation. This is consistent with the current result that the activation of dACC/msFC may be required for facilitating the information processing. Following this line of thought, the effective connectivity result would be thus needed to enable further understanding about the connectivity change between dACC/msFC with other FPN substrates.

5.2.3.2 The Changes of Effective Connectivity during Information Processing

The TFA was used to confirm the iTBS stimulation effect on the oscillation frequency bands during information processing. The TFA results supported that, during the information processing period (i.e., 150 – 300ms), the iTBS stimulation at dlPFC may increase the theta-band oscillation at frontal region of the brain during higher demand of rapid adative control. The ICoh analysis was conducted to further understand how the flows of theta- and alpha-band oscillations between the substrates of the CON and FPN were differentially changed across the task conditions after iTBS stimulation during information processing period. The pattern of

ICoh results during the timing of the information processing (150 – 300ms) was more complex than the results during the timing of the task-set implementation component (-200 – 0ms). There were four significant results found in two task conditions, incongruent trials of the single-task condition and congruent trials of the dual-task condition. Under the incongruent trials of the single-task condition, the connectivity changed after the iTBS stimulations at dlPFC (see Figure 4.2n, p. 97). The other three differences found under the congruent trials of the dual-task condition after stimulating at aI/fO, aPFC and dlPFC (see Figures 4.2p, 4.2r and 4.2t, p. 100, 102 and 104). These results will be discussed in the following sections.

5.2.3.2.1 Lower set-maintenance demand while higher rapid-adaptive demand. Under the incongruent trials of the single-task condition after stimulations at dlPFC, increased information flows of the theta-band oscillation were sent from dFC to dACC/msFC and from dACC/msFC to aPFC and dlPFC (see Figure 4.2n, p. 97). There are two observations in the connectivity change under higher demand of rapid-adaptive. First, the activation of dlPFC may play the key role to alter connectivity changes for the demand of rapid-adaptive. Under incongruent trials of single-task condition, only the Flanker task was required to be completed. Though there was the task-set of the Flanker task to be maintained, the CON and FPN should be engaged to process the targeted information of the targeted arrow form the distraction of the peripheral incongruent information. Unlike the task-set implementation facilitated by aI/fO of the CON, dlPFC of the FPN would be responsible for processing the moment-to-moment information of trials. It seemed that the substrates altering the connectivity changes may shift from one to another based on the cognitive demands required.

Second, increased connectivity between dlPFC and dACC/msFC was involved after stimulating at dlPFC. As discussed, to process the targeted information of the targeted arrow form the distraction, dlPFC may be modulated to enhance the signal of the target arrow. A sustained task-set information would be needed to update dlPFC. It concurs with current ICoh results that the increased theta-band oscillation sent from dACC/msFC to dlPFC (see Figure 4.2n, p. 97). Furthermore, the activation of dlPFC also increased the information sent from dFC to dACC/msFC. The activation of dFC was related to the trial initiation signal (Dosenbach et al., 2006, 2007 & 2008) while it did not send the signal to the dlPFC. It indicated that this increased flow of the theta-band oscillation may not be the cue for the dlPFC to process the stimulus timely. Instead, it may send the information of the initiation of trials to dACC/msFC for strengthen the signal of target stimulus monitored by dlPFC.

5.2.3.2.2 Higher set-maintenance demand while lower rapid-adaptive demand. Under the congruent trials of the dual-task condition, the changes of information flow of the alpha-band oscillation were found in two stimulation sites of the CON, aI/fO, and aPFC, and one stimulation site of the FPN, dlPFC. For the aI/fO stimulation, the information flows mainly increased the connection between the aI/fO with the other substrates of the CON. The aI/fO sent more information to dACC/msFC while it concurrently received from aPFC (see Figure 4.2p, p. 100). The increase of information flows was also found from dlPFC to aPFC. However, apart from sending more information to aPFC, dlPFC, less information was sent to the other within- and between-network substrates which included aI/fO, dACC/msFC, dFC, and IPS. Also, dlPFC received less information from the substrates of the CON, aPFC, and dACC/msFC. Less information was sent from dACC/msFC to aPFC. This suggests that the stimulation of aI/fO only facilitated the cooperation between aI/fO itself and the substrates of the CON and reduced almost all interactions between the dlPFC and other substrates, including the CON substrates, aI/fO, dACC/msFC, and aPFC, and the FPN substrates, dFC and IPS. It seems that under high set-maintenance demand while low rapid-adaptive demand, aI/fO may try to be more dominant to process the additional task-set. This phenomenon may find also in congruent trials of dual-task condition after stimulating at aPFC and dlPFC. After iTBS stimulations at aPFC, less information flow was sent from dACC/msFC to aPFC and also dlPFC (see Figure 4.2r, p. 102). The decrease of these two flows was also found after the stimulation was applied to aI/fO. As discussed, dACC/msFC might work with dlPFC to strengthen the signal of upcoming target information which may my necessary during congruent trials situation, that all information from the stimulus was aligned. Hence, both aI/fO and aPFC alter the connectivity between dACC/msFC and dlPFC to decrease the unnecessary process. Besides, the connectivity changes that altered by aPFC seemed overlap with the change altered by aI/fO under dual-task condition. aPFC probably serves as an assistant of aI/fO to manage part of the connectivity changes with immediately reacting to the congruency of a trial from the stimulus. This speculation was based on the suggestion made in previous studies that aPFC may be responsible to plan complex task-set such as task-switch paradigm (Braver et al., 2003), or paradigm with prolonged pre-stimulus interval (Sakai & Passingham, 2003). It indicated that aPFC may need to monitor the task-set with the update from the trial information. Hence, during the Flanker task, aPFC may alter the "strategy" when the trial was known whether it was congruent or incongruent situation. For the condition after stimulating at dlPFC, increased information flows were shown to send from aI/fO to dlPFC and sent from aPFC to aI/fO (see Figure 4.2t, p. 104). Interestingly, the increased information flows from aPFC to aI/fO were also found after stimulating aI/fO. The only difference was that the dlPFC received more information from aI/fO after stimulating at dlPFC while dlPFC sent less information to aI/fO (see Figure 4.2t, p. 104) after iTBS stimulations at aI/fO. It indicates that aI/fO may engage in processing of the additional task-set while the dlPFC actively receive information from aI/fO. To sum up, during information processing under higher set-maintenance demand while low rapid-adaptive demand, these changes of connectivity may probably tend to increase connectivity within the CON while decrease connectivity between CON and FPN, and also within the FPN. Their seemed aI/fO may become more dominant to maintain the additional task-set information. While the activation of aPFC and dlPFC may also change the connectivity between dual networks, these two substrates seemed to coordinate part of connectivity changes altered by aI/fO. This supports that, even during the information period, the dominant role would be based on the cognitive demand required. If the set-maintenance demand was higher, aI/fO of the CON may become more dominant to handle the task-set information first.

5.2.3.3 Differential Effect of aI/fO and dlPFC on Effective Connectivity during Information Processing

Consistent with previous studies, the changes of connectivity between aI/fO and dlPFC with other substrates may be related to the information processing (Chand & Dhamala, 2017; Sheffield et al., 2016). These studies tried to demonstrate the influential effect of aI/fO and dlPFC by correlating the overall task performance with task-state functional connectivity between aI/fO or dlPFC and substrates of other brain networks. For example, Sheffield et al. (2016) demonstrated the influential effect aI/fO with the overall performance score of five different tasks. The connectivity between each substrate of the CON and FPN, and substrates of other networks was also computed. The connectivity score was then used to predict the overall performance with linear regression model. The results revealed that only connectivity of aI/fO may predict the overall cognitive performance. It seemed that the aI/fO may have influence on processing the task relevant information while some other studies found dlPFC could be influential (Chand & Dhamala, 2017). However, previous studies, with using overall performance, may not discriminate the different process that would be altered by aI/fO or dlPFC. The current study may provide new evidence on the direct effect of aI/fO and dlPFC on the information processing. Furthermore, the current result showed that aI/fO and dlPFC may have different influence on situation with varied demand of set-maintenance and rapid-adaptive control. Under incongruent trials of single-task condition, dlPFC may alter the connectivity changes, especially between the dlPFC itself and dACC/msFC, to facilitate the rapid-adaptive control. Under congruent trials in the dual-task condition, though dlPFC may also alter the connectivity changes, aI/fO may have more influence on increasing the within connectivity of the CON to facilitate the set-maintenance control. It indicated that, during information processing, the influential effect of each substrate on the connectivity changes was highly dependent on the task demand while it may not be only handled by the FPN.

5.2.3.4 The Impact of Task Difficulty on Connectivity Change between dlPFC and dACC/msFC

The connectivity changes between dlPFC and dACC/msFC may relate to the task difficulty. The difficulty level of a task was suggested to be encoded at dACC/msFC

(Wisniewski et al., 2015). Wisniewski and colleagues (2015) used voluntary task-set selection method that allowed the participant to choose the task they perform based on the difficulty of the task. Hence, during task selection period, the information of task-set difficulty may be triggered for the choice reference. The results compared the brain activity across three level of task difficult and found only activation at dACC/msFC. Aligned with the results obtained in this study, the connectivity between dlPFC and dACC/msFC was found to increase during incongruent trials of single-task while it was found to decrease during congruent trials of dual-task. It may support that, during information processing, the increased connectivity between dlPFC and dACC/msFC may be required for higher rapid-adaptive demand. Though both aI/fO and dACC/msFC were related to task-set maintenance (Dosenbach et al., 2006, 2007 & 2008), dACC/msFC may be more sensitive to the rapid-adaptive demand of task-set while the aI/fO may be more sensitive to the set-maintenance demand of task-set.

5.3 General Discussion

5.3.1 Flexibility of dlPFC to Integrate a Wide Range of Information

The current results showed that, across different task demand condition or stimulation condition, dlPFC was highly flexible to adapt different information in order to facilitate the process of the corresponding task demand. For example, during task-set implementation under high set-maintenance and rapid-adaptive demand, the connectivity of dlPFC was altered by aI/fO and it increased three information flows from aI/fO, aPFC and dFC (see Figure 4.2i, p. 86). It seems to integrate the trial initiation information from dFC and the task-set planning from aPFC. During information processing under low set-maintenance and high rapid-adaptive demand, the connectivity of dlPFC was altered by dlPFC itself and it increased information flow from dACC/msFC to process high demand of rapid-adaptive control (see Figure 4.2n, p. 97). Another situation was that, under high demand of set-maintenance while low demand of rapid-adaptive, it actively received information from aI/fO and decreased the connectivity with other substrates (see Figure 4.2p, p. 100). It demonstrated that dlPFC may be a “good receiver” to control the adaption of appropriate information from both CON and FPN substrates. Cole (2013) demonstrated that the variability of between-network connectivity of the FPN was the highest among distinct brain networks across 64 different types of task-sets. It implied that FPN may connect with other networks flexibly to perform varied task. The current study may provide additional evidence that the flexibility of the FPN may be due to the changes of connectivity of dlPFC and other substrates in order to receive and integrate different types of information.

5.3.2 The Temporary Modulation of aI/fO on dlPFC

Under certain situation, especially high demand of set-maintenance, aI/fO may through dlPFC alter the connectivity within the FPN, or between the CON and FPN. The current results showed that during both task-set implementation (see Figure 4.2i, p.86) and information processing (see Figure 4.2p, p. 100), the connectivity changes of dlPFC were highly changed after stimulating at aI/fO. Under high set-maintenance and rapid-adaptive demand, aI/fO increased information flows from aPFC and dFC to dlPFC (see Figure 4.2i, p. 86). On the other hand, under high set-maintenance but low rapid-adaptive demand, aI/fO decreased the connectivity between dlPFC and aI/fO, aPFC, dACC/msFC, dFC and IPS (see Figure 4.2p, p. 100), It seemed, especially during high demand of set-maintenance control, aI/fO may temporary change both between and within network connectivity to manipulate the information processed by dlPFC.

5.3.3 Task-set Related Theta-band Oscillation and Trial Information Related Alpha-band Oscillation

The ICoh analysis, during task-set implementation, revealed only changes of information flows in only the theta-band oscillation but not the alpha-band oscillation. It implies that the theta-band oscillation may relate to the process of task-set information. There were a number of EEG studies that showed extra task-set demands may influence the alpha-band and theta-band oscillations (Lin et al., 2011; Magosso et al., 2019; Sauseng et al., 2006; Shaw et al., 2019; Wang et al., 2018). It showed the effect of the alpha- and theta-band oscillations on processing task-set related information. Most of the previous studies measured average EEG oscillation across the specific condition (Magosso et al., 2019; Sauseng et al., 2006; Shaw et al., 2019) while some of them provided temporal information of EEG oscillation without in-depth discussion on the task-set implementation period (Lin et al., 2011; Wang et al., 2018). Furthermore, in the current study, during information processing period, the connectivity changes with the theta-band oscillation were also found under incongruent trials of single-task condition. Though this condition had lower task-set demand, as discussed, the key component of this process should be the task-set that sent from dACC/msFC to dlPFC for monitoring task difficulty (see Figure 4.2n, p. 97). It matched with the speculation that the theta-band oscillation may be more relate to the task-set information. For the alpha-band oscillation, it was mainly found during information processing under congruent trials of dual-task condition. The demand of processing trial information was lower under congruent trials compared with incongruent. The results revealed a number of decreased connectivity flows of alpha-band oscillation during low rapid-adaptive demand situation. Hence, it was speculated that the alpha-band oscillation may relate to the processing of the moment-to-moment information.

5.3.4 No Significant Changes of Effective Connectivity Found under Both High Set-maintenance and Rapid-adaptive Demand During Information Processing

Last but not least, the behaviour results showed enhancement in the incongruent trials of the dual-task condition after the iTBS stimulations at aI/fO and dlPFC while the ERP and ICoh results may not be totally consistent with each other. The ICoh results seemed to explain that, after stimulating at aI/fO, the changes of network connectivity may facilitate the incongruent trials of the dual-task condition during task-set implementation. However, the current results may not support the enhancement for the situation after iTBS stimulations were applied at dlPFC. Although it was hypothesised that the dlPFC may highly influence the network connectivity under both high set-maintenance and rapid adaptive demand during the information processing period. However, it only showed the effect in either high set-maintenance demand or high rapid adaptive demand situation. One of the possible explanations was that, during this condition, highly cooperation between the aI/fO and dlPFC was found. During the high information processing period, the aI/fO may be much more dominant to handle high set-maintenance demand while the dlPFC may be much more dominant to handle high rapid-adaptive demand. Therefore, when both high set-maintenance demand and high rapid adaptive demand happened, the cooperation would be relatively complex and, hence, the variation of change during this period would be relatively high. Unlike the task-set implementation period, the process would be relatively unique to implement the task-set. However, the situation during the information processing had high variation of change and, hence, the information flow across networks would be difficult to be measured. Cole et al. (2013) demonstrated that the FPN had the highest variation of connectivity changes across different brain networks to handle the change of task-set. The high variation of connectivity changes may be the reason why statistically significant results could not be obtained under high set-maintenance demand and high rapid adaptive demand during the information processing period. The other possible reason was that the enhancement after stimulating, dlPFC may happen in the other processes, such as the decision making or execution period, and may not be reflected in earlier stages during task-set implementation and information processing.

5.4 Clinical Implications

The current study observed the influence of different network substrates of the CON and FPN on the top-control performance during different processes. It may provide new understanding about different top-down control processes in terms of the two networks. It may help to understand different top-down training in more detail. For example, dual-task training was usually used. The current study showed that the extra task-set may have influence on both the CON and FPN networks at different time points. Hence, it could deliver a new aspect to better select the appropriate training strategy.

Although this study focused on healthy young participants, it may offer a foundation for further investigating different situations that may face top-down control difficulties. Mild cognitive impairment (MCI) and Alzheimer's disease (AD) would be examples. There were a number of studies that found decreased within-network and between-network connectivity in the CON and FPN during ageing (Geerligs et al., 2015; Lee et al., 2016; Varangis et al., 2019; Xie et al., 2012). The current study may help to further investigate which cognitive processes would be affected by the changes of the connectivity in MCI or AD. Hence, it would allow to better understand a wide range of top-down control related diseases.

Furthermore, the iTBS stimulation in the current study provided new evidence about the effect of different network substrates of the CON and FPN on subsequent top-down performance. It may cooperate with the current clinical training to facilitate the training effect. However, the stimulation used in the current study was under only the exploratory stage for short term effect. Further investigations on stimulation protocol, dosage or even stimulation time would be needed.

CHAPTER SIX

CONCLUSION

6.1 Main Findings

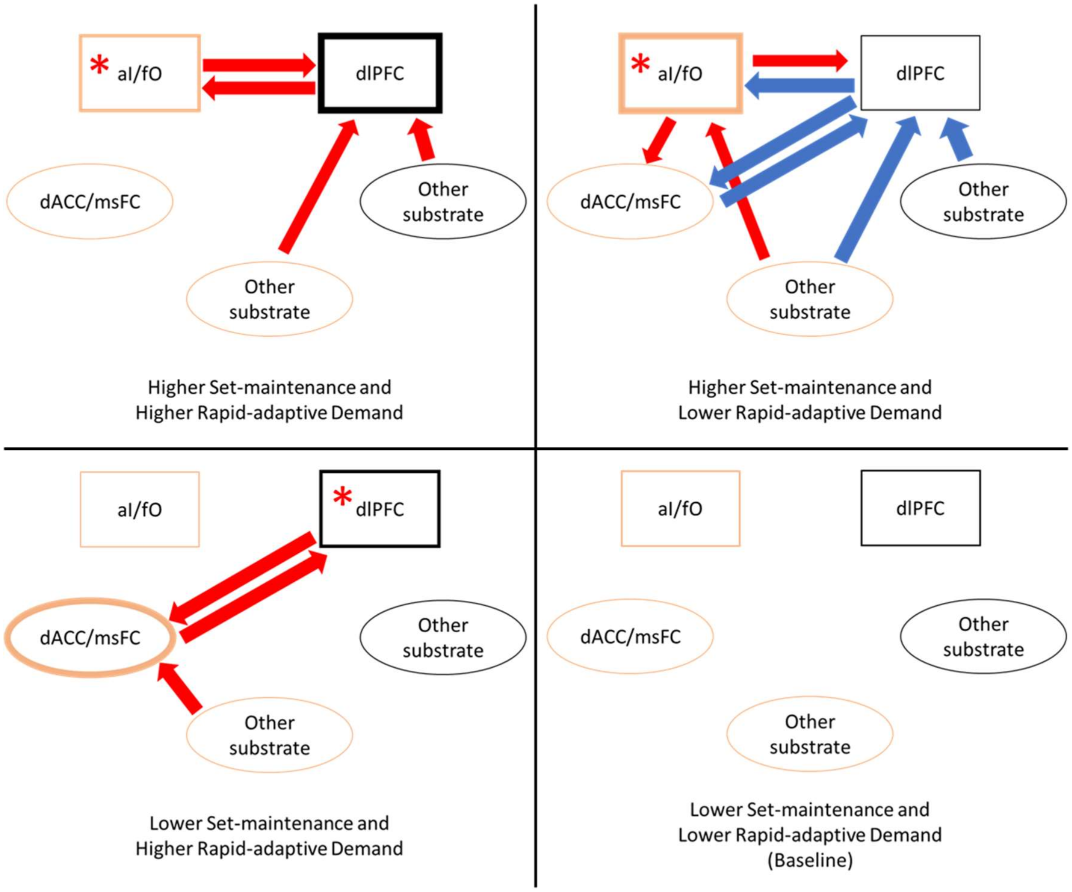
Study One demonstrated the effect of iTBS stimulation at aI/fO of the CON that facilitated the top-down performance of Flanker task under incongruent trials of dual-task condition while the iTBS stimulation at dACC/msFC and aPFC of the CON did not find this facilitation effect. It showed that aI/fO highly influenced both set-maintenance control and rapid-adaptive performance. The activation of aI/fO may not only facilitate the implementation and maintenance of extra task-set, but also facilitate the processing of trial information. Hence, the Flanker task performance could be enhanced in term of shorter reaction time.

In Study Two, the behavioural results further showed the facilitation effect of top-down performance after stimulating at aI/fO of the CON and stimulating at dlPFC of the FPN. For both stimulation conditions, the results revealed a shorter reaction time was found in the incongruent trials of the dual-task compared with the single-task condition. This indicated that both aI/fO of the CON and dlPFC of the FPN may facilitate the task performance under high set-maintenance and rapid-adaptive demand situations. While the CON and the FPN should be responsible for the set-maintenance and rapid-adaptive respectively and separately, it seemed that they may cooperate to handle the situation with high set-maintenance and rapid-adaptive demand.

The ERP and ICoh analysis were further used to explore the enhancement effect from the stimulation of aI/fO and dlPFC during two different processes, task-set implementation and information processing. Figure 6.1 (p. 142) shows the conceptual schema that summarize the main findings about the flow of the neural signals among representative neural substrates of the CON and FPN under higher and lower levels of set-maintenance and rapid-adaptive demands as discussed in Chapter 5. Under high set-maintenance and high rapid-adaptive condition, the activation of aI/fO may increase the between-network connectivity to handle additional process. It increased the information flows between aI/O and dlPFC. Also, more information flows were sent from aI/fO to dFC and also from dlPFC to aPFC. To handle additional information for other substrates, a stronger activation may be required by dlPFC, which was supported by more negative-going SPN component under this period of time. It seemed that aI/fO would be dominant, under high set-maintenance and rapid-adaptive demand, in order to manipulate the changes of between network connectivity. The aI/fO should be the key substrate to monitor task-set implementation while it would need help from dlPFC under high set-maintenance demand situations. Under higher rapid-adaptive while lower set-maintenance control condition, the activation of dlPFC increased between-network connectivity with involved dACC/msFC and aPFC during the information processing period. The dlPFC of FPN appear to play a more dominant role to alter the functional connectivity and may have received help from dACC/msFC of the CON to handle additional rapid-adaptive demands. The less negative-going N1 found after stimulation at dACC/msFC which may be reflected the additional resources may be required to process rapid-adaptive information. However, under only higher set-maintenance demand while lower rapid-adaptive demand, aI/fO showed a much more dominant role to manage additional task-set information. Under higher set-maintenance demand, aI/fO increased information flows between aI/fO itself and the within- and between-network substrates including dACC/msFC, aPFC, and dlPFC, while it decreased the information flows between dlPFC and other substrates including aI/fO, dACC/msFC, dFC, and IPS. During the information processing period, the cooperation between the CON and FPN seemed to be much more flexible in that dlPFC became the leading role under high rapid-adaptive demand while aI/fO became the leading role under high set-maintenance demand.

Figure 6.1

A concept schema shows the changes of effective connectivity between the neural substrates of the CON and FPN under higher and lower demands of set-maintenance and rapid-adaptive control conditions



Note. The substrates of the CON show in orange while the substrates of the FPN show in black. Red arrows represent increased flow of oscillations while blue arrows represent decreased flow of oscillations. The substrates show in square is the suggest substrate that may alter network connectivity and the star shows the substrates that is more dominant under corresponding condition. Thinker boundary of the substrates represent stronger activation required under corresponding situation

To conclude, the current study supported the influential effect of aI/fO of the CON and dlPFC of FPN on set-maintenance control and repaid-adaptive control respectively. Additionally, the current results suggested aI/fO and dlPFC may have differential effect on task-set implementation (-200 – 0ms) and information processing (150 – 300ms). It indicated they may alter the connectivity between the CON and FPN to handle corresponding task demand. The distinct role of three key substrates of dual networks were also discussed. First, aI/fO should be more responsible to handle task-set related demands. Additional task-set information may lead aI/fO to alter the between- and within-network connectivity changes with the help of dlPFC while dlPFC may be a flexible substrate to adapt different information for achieve wide range of task condition. For dACC/msFC, it may be sensitive to the task difficulty and may be reactive to dlPFC under high rapid-adaptive demand situation.

6.2 Limitations

6.2.1 The Laterality of Brain Function

The current study did not examine the laterality of brain function. Only right hemisphere substrates were selected as the stimulation sites. Some studies have suggested that there are brain regions which may have different connectivity between the two hemispheres, such as Kann et al. (2016). They demonstrated the aI found lateralised connectivity. This implies that the stimulation on different cortical hemispheres may lead to different connectivity.

However, the laterality of brain functions was rarely discussed in most of the connectivity of networks (Cole et al., 2013; Dosenbach et al., 2008; Gordon et al., 2018). Also, Dosenbach et al. (2006) showed that almost symmetrical activation patterns are in the CON and FPN. The stimulation sites selected, including right aI/fO, dACC/msFC, aPFC, dlPFC, and dFC, showed consistent activation patterns across different types of tasks (Dosenbach et al., 2006). Therefore, the current study focused on the connectivity and functionality in the right hemisphere of the CON and FPN under the general situation.

6.2.2 Limited Number of Network Substrates in ICoh Model

As the sample size of the current study was relatively small, increasing the number of network substrates in ICoh may have significantly lowered the effect size. Therefore, only key regions of dual networks, the CON and FPN, were included. However, some other networks may have been involved in the changes of connectivity and influenced the top-down control performance. For example, it was suggested that a part of the dorsal-stream attention network may overlap with the FPN (Dosenbach et al., 2008). The current study limited the connectivity changes in the CON and the FPN, but it may not have shown the highly flexible changes of connectivity between dual networks and other networks. Further studies would need to have a larger sample size for testing the model of connectivity across different networks.

6.2.3 Limited Task Types Lowering the Generalisability of the Study

The current task designs used mainly the Flanker task and 2-back tasks while the results were focused on the performance of the Flanker task. The Flanker task and 2-back tasks share several similar characteristics that they are both cognitive with visual as input and bottom pressing as output. This arrangement may limit the changes of connectivity function that may require to engage with other networks. While the CON and FPN were task-general networks that may show similar activation patterns across different types of tasks (Cole et al., 2013; Dosenbach et al., 2006, 2007 & 2008; Gordon et al., 2018). On the other hand, the current study showed that, during the information processing of certain high cognitive demand situations, the connectivity between two networks may flexibly change based on the needs of the corresponding tasks. It is yet to be ascertained whether this flexible pattern may happen under only the combination of these two cognitive tasks with similar input and output characteristics. Further investigation could be conducted with reference to Dosenbach et al. (2006) by using different types of tasks, including different types of input, such as auditory, and different types of output, such as speech.

6.3 Future Studies

The current study provides initial evidence to understand the different patterns of connectivity change between dual top-down networks during different processes, task-set implementation and information processing, in order to handle various demands of set-maintenance and rapid-adaptive control. Further studies would be required to develop this area of knowledge.

First, single-pulse online stimulation study could be conducted. The offline iTBS stimulation used in the current study could facilitate the networks across the tasks. It may help to explore different processes across the tasks. However, it would be hard to understand how each of the processes may influence the subsequent performance after stimulating the target sites. Single-pulse online stimulation may provide a shorter time period of influence. A specific process could be investigated without the influence of other facilitated processes. The current study showed the influential effect of activation of dlPFC and aI/fO on the changes of the network connectivity. It is suggested to further investigate how these two substrates may differently affect the subsequence performance with facilitating different cognitive processes. It may provide extra detail on understanding the influence of aI/fO and dlPFC on different task performance through changing the connectivity of specific cognitive processes.

Second, participants with different types of top-down difficulties could be recruited. For example, participants with mild cognitive impairment (MCI) or Alzheimer’s disease (AD) were found to have decreased network connectivity between the CON and FPN (Geerligs et al., 2015; Lee et al., 2016; Varangis et al., 2019; Xie et al., 2012). However, the current method may help to investigate whether the changes of connectivity may be due to difficulties in specific processes or overall performance. It could provide extra features to understand the deterioration mechanism and provide more tailor-made training to each type of top-down difficulties.

Moreover, the dosage of iTBS stimulation on aI/fO or dlPFC should be further explored to test the long-term effect on healthy participants first. While the current study showed the temporarily facilitation effect of aI/fO and dlPFC stimulation on the subsequent performance, a similar stimulation method may be used to facilitate and assist the training of those with top-down difficulties. Some studies examined the influence of the stimulating dlPFC on long-term top-down control performance (Holczer et al., 2020) while there was a lack of investigations about aI/fO TMS stimulation. A random controlled trials experiment could be first conducted to explore the different long-term effect elicited by aI/fO and dlPFC before further testing the application on the training of other targeted participants.

REFERENCES

Axelrod, B. N., Goldman, R. S., & Woodard, J. L. (1992). Interrater reliability in scoring the Wisconsin card sorting test. *Clinical Neuropsychologist*, *6*(2), 143–155. https://doi.org/10.1080/13854049208401851

Barceló, F., Muñoz-Céspedes, J. M., Pozo, M. A., & Rubia, F. J. (2000). Attentional set shifting modulates the target P3b Response in the Wisconsin card sorting test. *Neuropsychologia*, *38*(10), 1342–1355. https://doi.org/10.1016/s0028-3932(00)00046-4

Beaty, R. E., Benedek, M., Barry Kaufman, S., & Silvia, P. J. (2015). Default and Executive Network Coupling Supports Creative Idea Production. *Scientific Reports*, *5*(1). https://doi.org/10.1038/srep10964

Braver, T. S. (2012). The variable nature of cognitive control: a dual mechanisms framework. *Trends in Cognitive Sciences*, *16*(2), 106–113. https://doi.org/10.1016/j.tics.2011.12.010

Braver, T. S., Reynolds, J. R., & Donaldson, D. I. (2003). Neural Mechanisms of Transient and Sustained Cognitive Control during Task Switching. *Neuron*, *39*(4), 713–726. https://doi.org/10.1016/s0896-6273(03)00466-5

Brunia, C. H. M., van Boxtel, G. J. M., & Böcker, K. B. E. (2012). Negative Slow Waves as Indices of Anticipation: The Bereitschaftspotential, the Contingent Negative

Variation, and the Stimulus-Preceding Negativity. *The Oxford Handbook of Event-Related Potential Components*. https://doi.org/10.1093/oxfordhb/9780195374148.013.0108

Bueno, M., Fort, A., Francois, M., Ndiaye, D., Deleurence, P., & Fabrigoule, C. (2013). Effectiveness of a Forward Collision Warning System in simple and in dual task from an electrophysiological perspective. *Neuroscience Letters*, *541*, 219–223. https://doi.org/10.1016/j.neulet.2013.02.030

Chand, G. B., & Dhamala, M. (2017). Interactions between the anterior cingulate-insula network and the fronto-parietal network during perceptual decision-making. *NeuroImage*, *152*, 381–389. https://doi.org/10.1016/j.neuroimage.2017.03.014

Chen, J., Zhou, C., Wu, B., Wang, Y., Li, Q., Wei, Y., Yang, D., Mu, J., Zhu, D., Zou, D., & Xie, P. (2013). Left versus right repetitive transcranial magnetic stimulation in treating major depression: A meta-analysis of randomised controlled trials. *Psychiatry Research*, *210*(3), 1260–1264. https://doi.org/10.1016/j.psychres.2013.09.007

Chung, S. W., Hill, A. T., Rogasch, N. C., Hoy, K. E., & Fitzgerald, P. B. (2016). Use of theta-burst stimulation in changing excitability of motor cortex: A systematic review and meta-analysis. *Neuroscience & Biobehavioral Reviews*, *63*, 43–64. https://doi.org/10.1016/j.neubiorev.2016.01.008

Cole, M. W., Ito, T., Cocuzza, C., & Sanchez-Romero, R. (2021). The Functional Relevance of Task-State Functional Connectivity. *The Journal of Neuroscience*, *41*(12), 2684–2702. https://doi.org/10.1523/jneurosci.1713-20.2021

Cole, M. W., Reynolds, J. R., Power, J. D., Repovs, G., Anticevic, A., & Braver, T. S. (2013). Multi-task connectivity reveals flexible hubs for adaptive task control. *Nature Neuroscience*, *16*(9), 1348–1355. https://doi.org/10.1038/nn.3470

D'Elia, L. F., Satz, P., Uchiyama, C. L., & White, T. (1996). *Color Trails Test: professional manual*. Odessa, FL: Psychological Assessment Resources.

De Ridder, D., Vanneste, S., Kovacs, S., Sunaert, S., & Dom, G. (2011). Transient alcohol craving suppression by rTMS of dorsal anterior cingulate: An fMRI and LORETA EEG study. *Neuroscience Letters*, *496*(1), 5–10. https://doi.org/10.1016/j.neulet.2011.03.074

Delorme, A., & Makeig, S. (2004). EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *J. Neurosci. Methods,* *134*, 9–21. doi: 10.1016/j.jneumeth.2003.10.009

Doallo, S., Lorenzo-López, L., Vizoso, C., Rodríguez Holguín, S., Amenedo, E., Bará, S., & Cadaveira, F. (2005). Modulations of the visual N1 component of event-related potentials by central and peripheral cueing. *Clinical Neurophysiology*, *116*(4), 807–820. https://doi.org/10.1016/j.clinph.2004.11.013

Dosenbach, N. U. F., Fair, D. A., Miezin, F. M., Cohen, A. L., Wenger, K. K., Dosenbach, R. A. T., Fox, M. D., Snyder, A. Z., Vincent, J. L., Raichle, M. E., Schlaggar, B. L., & Petersen, S. E. (2007). Distinct brain networks for adaptive and stable task control in humans. *Proceedings of the National Academy of Sciences*, *104*(26), 11073–11078. https://doi.org/10.1073/pnas.0704320104

Dosenbach, N. U., Fair, D. A., Cohen, A. L., Schlaggar, B. L., & Petersen, S. E. (2008). A dual-networks architecture of top-down control. *Trends in Cognitive Sciences*, *12*(3), 99–105. https://doi.org/10.1016/j.tics.2008.01.001

Dosenbach, N. U., Visscher, K. M., Palmer, E. D., Miezin, F. M., Wenger, K. K., Kang, H. C., Burgund, E. D., Grimes, A. L., Schlaggar, B. L., & Petersen, S. E. (2006). A Core System for the Implementation of Task Sets. *Neuron*, *50*(5), 799–812. https://doi.org/10.1016/j.neuron.2006.04.031

Egner, T. (2007). Congruency sequence effects and cognitive control. *Cognitive, Affective, & Behavioral Neuroscience*, *7*(4), 380–390. https://doi.org/10.3758/cabn.7.4.380

Fernandez Guerrero, A., & Achermann, P. (2018). Intracortical Causal Information Flow of Oscillatory Activity (Effective Connectivity) at the Sleep Onset Transition. *Frontiers in Neuroscience*, *12*. https://doi.org/10.3389/fnins.2018.00912

Franzen, M. D., Tishelman, A. C., Sharp, B. H., & Friedman, A. G. (1987). An investigation of the test-retest reliability of the stroop colorword test across two intervals. *Archives of Clinical Neuropsychology*, *2*(3), 265–272. https://doi.org/10.1093/arclin/2.3.265

Geerligs, L., Renken, R. J., Saliasi, E., Maurits, N. M., & Lorist, M. M. (2014). A Brain-Wide Study of Age-Related Changes in Functional Connectivity. *Cerebral Cortex*, *25*(7), 1987–1999. https://doi.org/10.1093/cercor/bhu012

Gherri, E., & Eimer, M. (2011). Active Listening Impairs Visual Perception and Selectivity: An ERP Study of Auditory Dual-task Costs on Visual Attention. *Journal of Cognitive Neuroscience*, *23*(4), 832–844. https://doi.org/10.1162/jocn.2010.21468

Gordon, E. M., Laumann, T. O., Adeyemo, B., Gilmore, A. W., Nelson, S. M., Dosenbach, N. U., & Petersen, S. E. (2017). Individual-specific features of brain systems identified with resting state functional correlations. *NeuroImage*, *146*, 918–939. https://doi.org/10.1016/j.neuroimage.2016.08.032

Gordon, E. M., Lynch, C. J., Gratton, C., Laumann, T. O., Gilmore, A. W., Greene, D. J., Ortega, M., Nguyen, A. L., Schlaggar, B. L., Petersen, S. E., Dosenbach, N. U., &

Nelson, S. M. (2018). Three Distinct Sets of Connector Hubs Integrate Human Brain Function. *Cell Reports*, *24*(7), 1687–1695.e4. https://doi.org/10.1016/j.celrep.2018.07.050

Gratton, C., Laumann, T., Gordon, E., Adeyemo, B., & Petersen, S. (2016). Evidence for Two Independent Factors that Modify Brain Networks to Meet Task Goals. *Cell Reports*, *17*(5), 1276–1288. https://doi.org/10.1016/j.celrep.2016.10.002

Gratton, C., Lee, T. G., Nomura, E. M., & D'Esposito, M. (2013). The effect of theta-burst TMS on cognitive control networks measured with resting state fMRI. *Frontiers in Systems Neuroscience*, *7*. https://doi.org/10.3389/fnsys.2013.00124

Gratton, C., Lee, T. G., Nomura, E. M., & D'Esposito, M. (2014). Perfusion MRI Indexes Variability in the Functional Brain Effects of Theta-Burst Transcranial Magnetic Stimulation. *PLoS ONE*, *9*(7), e101430. https://doi.org/10.1371/journal.pone.0101430

Gunner, J. H., Miele, A. S., Lynch, J. K., & McCaffrey, R. J. (2012). Performance of Non-neurological Older Adults on the Wisconsin Card Sorting Test and the Stroop Color-Word Test: Normal Variability or Cognitive Impairment? *Archives of Clinical Neuropsychology*, *27*(4), 398–405. https://doi.org/10.1093/arclin/acs047

Hillyard, S. A., & Anllo-Vento, L. (1998). Event-related brain potentials in the study of visual selective attention. *Proceedings of the National Academy of Sciences*, *95*(3), 781–787. https://doi.org/10.1073/pnas.95.3.781

Hoang, I., Ranchet, M., Derollepot, R., Moreau, F., & Paire-Ficout, L. (2020). Measuring the cognitive workload during dual-task walking in young adults: A combination of neurophysiological and subjective measures. *Frontiers in Human Neuroscience*, *14*. https://doi.org/10.3389/fnhum.2020.592532

Holczer, A., Németh, V. L., Vékony, T., Vécsei, L., Klivényi, P., & Must, A. (2020). Non-invasive brain stimulation in Alzheimer's Disease and mild cognitive impairment—A state-of-the-art review on methodological characteristics and stimulation parameters. *Frontiers in Human Neuroscience*, *14*. https://doi.org/10.3389/fnhum.2020.00179

Huaijian Zhang, Chavarriaga, R., Gheorghe, L., & del R Millan, J. (2013). Inferring driver's turning direction through detection of error related brain activity. *2013 35th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*. https://doi.org/10.1109/embc.2013.6609971

Ito, T., Kulkarni, K. R., Schultz, D. H., Mill, R. D., Chen, R. H., Solomyak, L. I., & Cole, M. W. (2017). Cognitive task information is transferred between brain regions via resting-state network topology. *Nature Communications*, *8*(1), 1027(2017). https://doi.org/10.1038/s41467-017-01000-w

Kang, M. S., DiRaddo, A., Logan, G. D., & Woodman, G. F. (2014). Electrophysiological evidence for preparatory reconfiguration before voluntary task switches but not cued task switches. *Psychonomic Bulletin & Review,* 21(2), 454–461. https://doi.org/10.3758/s13423-013-0499-8

Kann, S., Zhang, S., Manza, P., Leung, H. C., & Li, C. S. R. (2016). Hemispheric lateralization of resting-state functional connectivity of the anterior insula: association with age, gender, and a novelty-seeking trait. *Brain Connectivity*, *6*(9), 724–734. https://doi.org/10.1089/brain.2016.0443

Karayanidis, F., Whitson, L. R., Heathcote, A., & Michie, P. T. (2011). Variability in proactive and reactive cognitive control processes across the adult lifespan. *Frontiers in Psychology*, *2*. https://doi.org/10.3389/fpsyg.2011.00318

Keel, J. C., Smith, M. J., & Wassermann, E. M. (2001). A safety screening questionnaire for transcranial magnetic stimulation. *Clinical Neurophysiology*, *112*(4), 720. https://doi.org/10.1016/s1388-2457(00)00518-6

Kehrer, S., Kraft, A., Koch, S. P., Kathmann, N., Irlbacher, K., & Brandt, S. A. (2015). Timing of spatial priming within the fronto-parietal attention network: A TMS study.

Neuropsychologia, *74*, 30–36. https://doi.org/10.1016/j.neuropsychologia.2014.11.017

Kitaura, Y., Nishida, K., Yoshimura, M., Mii, H., Katsura, K., Ueda, S., Ikeda, S., Pascual-Marqui, R. D., Ishii, R., & Kinoshita, T. (2017). Functional localization and effective connectivity of cortical theta and alpha oscillatory activity during an attention task. *Clinical Neurophysiology Practice*, *2*, 193–200. https://doi.org/10.1016/j.cnp.2017.09.002

Kondo, H., Osaka, N., & Osaka, M. (2004). Cooperation of the anterior cingulate cortex and dorsolateral prefrontal cortex for attention shifting. *NeuroImage*, *23*(2), 670–679. https://doi.org/10.1016/j.neuroimage.2004.06.014

Kotani, Y., Ohgami, Y., Yoshida, N., Kiryu, S., & Inoue, Y. (2017). Anticipation process of the human brain measured by stimulus-preceding negativity (SPN). *The Journal of Physical Fitness and Sports Medicine*, *6*(1), 7–14. https://doi.org/10.7600/jpfsm.6.7

Lee, A., Tan, M., & Qiu, A. (2016). Distinct aging effects on functional networks in good and poor cognitive performers. *Frontiers in Aging Neuroscience*, *8*. https://doi.org/10.3389/fnagi.2016.00215

Leung, J. L. M., Lee, G. T. H., Lam, Y. H., Chan, R. C. C., & Wu, J. Y. M. (2011). The use of the Digit Span Test in screening for cognitive impairment in acute medical inpatients. *International Psychogeriatrics*, *23*(10), 1569–1574. https://doi.org/10.1017/s1041610211000792

Lin, C. T., Chen, S. A., Chiu, T. T., Lin, H. Z., & Ko, L. W. (2011). Spatial and temporal EEG dynamics of dual-task driving performance. *Journal of NeuroEngineering and Rehabilitation*, *8*(11). https://doi.org/10.1186/1743-0003-8-11

Little, C. E., & Woollacott, M. (2014). EEG measures reveal dual-task interference in postural performance in young adults. *Experimental Brain Research*, *233*(1), 27–37. https://doi.org/10.1007/s00221-014-4111-x

Lowe, C. J., Manocchio, F., Safati, A. B., & Hall, P. A. (2018). The effects of theta burst stimulation (TBS) targeting the prefrontal cortex on executive functioning: A systematic review and meta-analysis. *Neuropsychologia*, *111*, 344–359. https://doi.org/10.1016/j.neuropsychologia.2018.02.004

Magosso, E., de Crescenzio, F., Ricci, G., Piastra, S., & Ursino, M. (2019). EEG alpha power is modulated by attentional changes during cognitive tasks and virtual reality immersion. *Computational Intelligence and Neuroscience*, *2019*, 1–18. https://doi.org/10.1155/2019/7051079

Min, B. K., & Park, H. J. (2010). Task-related modulation of anterior theta and posterior alpha EEG reflects top-down preparation. *BMC Neuroscience, 11*(1), 79–79. https://doi.org/10.1186/1471-2202-11-79

Nielsen, T. R., Segers, K., Vanderaspoilden, V., Bekkhus-Wetterberg, P., Minthon, L., Pissiota, A., Bjørkløf, G. H., Beinhoff, U., Tsolaki, M., Gkioka, M., & Waldemar, G. (2018). Performance of middle-aged and elderly European minority and majority populations on a Cross-Cultural Neuropsychological Test Battery (CNTB). *The Clinical Neuropsychologist*, *32*(8), 1411–1430. https://doi.org/10.1080/13854046.2018.1430256

Nozawa, T., Sugiura, M., Yokoyama, R., Ihara, M., Kotozaki, Y., Miyauchi, C. M., Kanno, A., & Kawashima, R. (2014). Ongoing Activity in Temporally Coherent Networks Predicts Intra-Subject Fluctuation of Response Time to Sporadic Executive Control Demands. *PLoS ONE*, *9*(6), e99166. https://doi.org/10.1371/journal.pone.0099166

Pascual-Marqui, R. (2007). Discrete, 3D distributed, linear imaging methods of electric neuronal activity. Part 1: exact, zero error localization.

Pascual-Marqui, R., Biscay, R., Bosch-Bayard, J., Lehmann, D., Kochi, K., Yamada, N., Kinoshita, T., & Sadato, N. (2014). P17. Isolated effective coherence (iCoh) based on estimated electric neuronal activity using exact low resolution brain electromagnetic tomography (eLORETA). *Clinical Neurophysiology*, *125*(10), e46–e47. https://doi.org/10.1016/j.clinph.2014.06.018

Pascual-Marqui, R. D., Biscay, R. J., Bosch-Bayard, J., Lehmann, D., Kochi, K., Kinoshita, T., Yamada, N., & Sadato, N. (2014). Assessing direct paths of intracortical causal information flow of oscillatory activity with the isolated effective coherence (iCoh). *Frontiers in Human Neuroscience*, *8*. https://doi.org/10.3389/fnhum.2014.00448

Pascual-Marqui, R. D., Lehmann, D., Koukkou, M., Kochi, K., Anderer, P., Saletu, B., Tanaka, H., Hirata, K., John, E. R., Prichep, L., Biscay-Lirio, R., & Kinoshita, T. (2011). Assessing interactions in the brain with exact low-resolution electromagnetic tomography. *Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences*, *369*(1952), 3768–3784. https://doi.org/10.1098/rsta.2011.0081

Pillay, S., Durgerian, S., & Sabri, M. (2016). Perceptual demand and distraction interactions mediated by task-control networks. *NeuroImage*, *138*, 141–146. https://doi.org/10.1016/j.neuroimage.2016.05.077

Power, J., Cohen, A., Nelson, S., Wig, G., Barnes, K., Church, J., Vogel, A., Laumann, T., Miezin, F., Schlaggar, B., & Petersen, S. (2011). Functional Network Organization of the Human Brain. *Neuron*, *72*(4), 665–678. https://doi.org/10.1016/j.neuron.2011.09.006

Sakai, K., & Passingham, R. E. (2002). Prefrontal interactions reflect future task operations. *Nature Neuroscience*, *6*(1), 75–81. https://doi.org/10.1038/nn987

Sandrini, M., Umiltà, C., & Rusconi, E. (2011). The use of transcranial magnetic stimulation in cognitive neuroscience: A new synthesis of methodological issues. *Neuroscience & Biobehavioral Reviews*, *35*(3), 516–536. https://doi.org/10.1016/j.neubiorev.2010.06.005

Sauseng, P., Klimesch, W., Freunberger, R., Pecherstorfer, T., Hanslmayr, S., & Doppelmayr, M. (2005). Relevance of EEG alpha and theta oscillations during task switching. *Experimental Brain Research*, *170*(3), 295–301. https://doi.org/10.1007/s00221-005-0211-y

Shaw, E. P., Rietschel, J. C., Shuggi, I. M., Xu, Y., Chen, S., Miller, M. W., Hatfield, B. D., & Gentili, R. J. (2019). Cerebral cortical networking for mental workload assessment under various demands during dual-task walking. *Experimental Brain Research*, *237*(9), 2279–2295. https://doi.org/10.1007/s00221-019-05550-x

Sheffield, J. M., Repovs, G., Harms, M. P., Carter, C. S., Gold, J. M., MacDonald III, A. W., Daniel Ragland, J., Silverstein, S. M., Godwin, D., & Barch, D. M. (2015). Fronto-parietal and cingulo-opercular network integrity and cognition in health and schizophrenia. *Neuropsychologia*, *73*, 82–93. https://doi.org/10.1016/j.neuropsychologia.2015.05.006

Shine, J., Bissett, P., Bell, P., Koyejo, O., Balsters, J., Gorgolewski, K., Moodie, C., & Poldrack, R. (2016). The Dynamics of Functional Brain Networks: Integrated Network States during Cognitive Task Performance. *Neuron*, *92*(2), 544–554. https://doi.org/10.1016/j.neuron.2016.09.018

Singhal, A., Doerfling, P., & Fowler, B. (2002). Effects of a dual task on the N100-P200 complex and the early and late Nd attention waveforms. *Psychophysiology*, *39*(2), 236–245. https://doi.org/10.1111/1469-8986.3920236

Soutschek, A., Taylor, P. C. J., & Schubert, T. (2016). The role of the dorsal medial frontal cortex in central processing limitation: a transcranial magnetic stimulation study. *Experimental Brain Research*, *234*(9), 2447–2455. https://doi.org/10.1007/s00221-016-4649-x

Steinhauser, R., & Steinhauser, M. (2018). Preparatory brain activity in dual-tasking. *Neuropsychologia*, *114*, 32–40. https://doi.org/10.1016/j.neuropsychologia.2018.04.014

Steinmann, S., Amselberg, R., Cheng, B., Thomalla, G., Engel, A. K., Leicht, G., & Mulert, C. (2018). The role of functional and structural interhemispheric auditory connectivity for language lateralization - A combined EEG and DTI study. *Scientific Reports*, *8*(1). https://doi.org/10.1038/s41598-018-33586-6

Stuss, D., Floden, D., Alexander, M., Levine, B., & Katz, D. (2001). Stroop performance in focal lesion patients: dissociation of processes and frontal lobe lesion location. *Neuropsychologia*, *39*(8), 771–786. https://doi.org/10.1016/s0028-3932(01)00013-6

Theeuwes, J. (2010). Top–down and bottom–up control of visual selection. *Acta Psychologica*, *135*(2), 77–99. https://doi.org/10.1016/j.actpsy.2010.02.006

Tong, S., Thakor, N. V., & Thankor, N. V. (2009). *Quantitative EEG Analysis Methods and Clinical Applications*. Penguin Random House.

Van Boxtel, G. J., & Böcker, K. B. (2004). Cortical Measures of Anticipation. *Journal of Psychophysiology*, *18*(2/3), 61–76. https://doi.org/10.1027/0269-8803.18.23.61

Van den Heuvel, M. P., & Sporns, O. (2013). Network hubs in the human brain. *Trends in Cognitive Sciences*, *17*(12), 683–696. https://doi.org/10.1016/j.tics.2013.09.012

Van der Elst, W., van Boxtel, M. P. J., van Breukelen, G. J. P., & Jolles, J. (2006). The Stroop Color-Word Test. *Assessment*, *13*(1), 62–79. https://doi.org/10.1177/1073191105283427

Vanderhasselt, M.-A., de Raedt, R., Leyman, L., & Baeken, C. (2009). Acute effects of repetitive transcranial magnetic stimulation on attentional control are related to antidepressant outcomes. *Journal of Psychiatry & Neuroscience*, *34*(2), 119–126.

Varangis, E., Habeck, C. G., Razlighi, Q. R., & Stern, Y. (2019). The Effect of Aging on Resting State Connectivity of Predefined Networks in the Brain. *Frontiers in Aging Neuroscience*, *11*, 234. https://doi.org/10.3389/fnagi.2019.00234

Wang, Y. K., Jung, T. P., & Lin, C. T. (2018). Theta and Alpha Oscillations in Attentional Interaction during Distracted Driving. *Frontiers in Behavioral Neuroscience*, *12*, 3. https://doi.org/10.3389/fnbeh.2018.00003

Waters, G. S., & Caplan, D. (2003). The reliability and stability of verbal working memory measures. *Behavior Research Methods, Instruments, & Computers*, *35*(4), 550–564. https://doi.org/10.3758/bf03195534

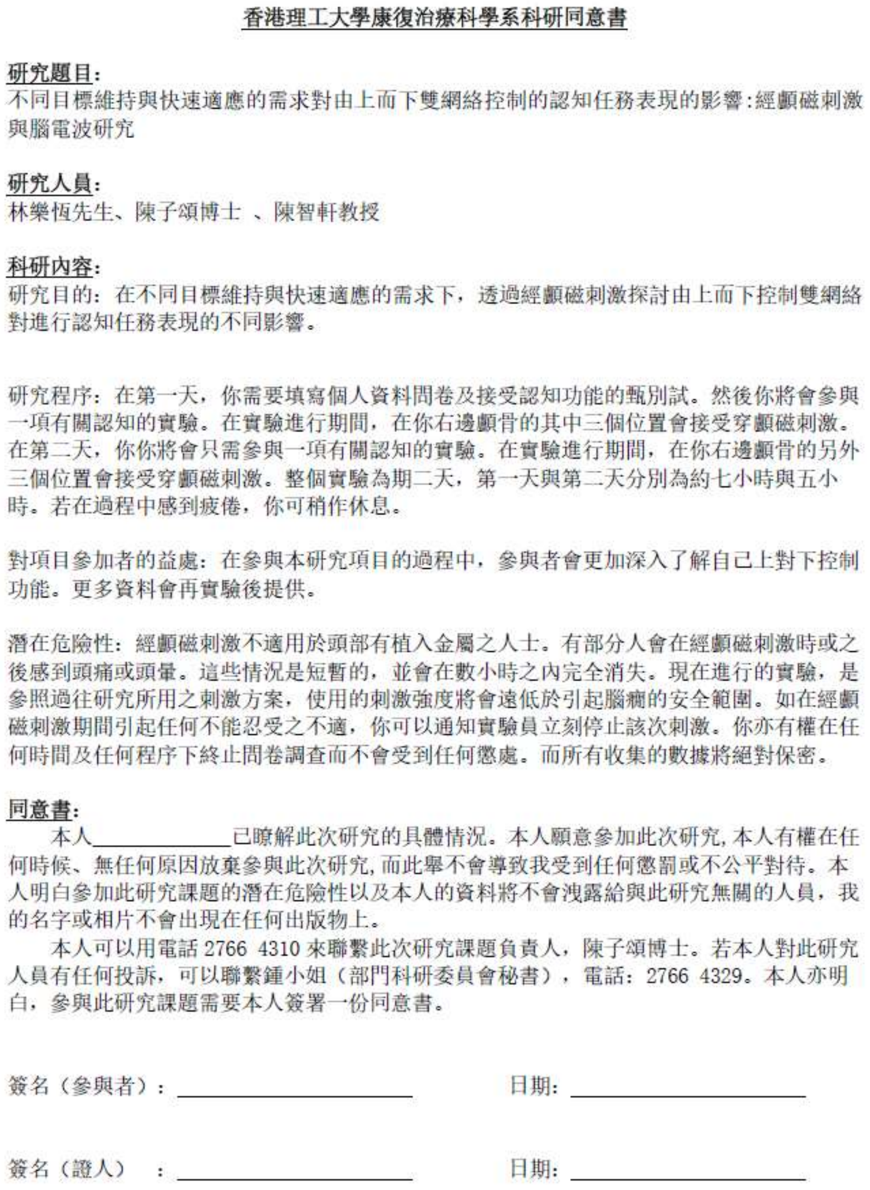
Weinbach, N., & Henik, A. (2012). The relationship between alertness and executive control. *Journal of Experimental Psychology: Human Perception and Performance*, *38*(6), 1530–1540. https://doi.org/10.1037/a0027875

Xie, C., Bai, F., Yu, H., Shi, Y., Yuan, Y., Chen, G., Li, W., Chen, G., Zhang, Z., & Li, S. J. (2012). Abnormal insula functional network is associated with episodic memory decline in amnestic mild cognitive impairment. *NeuroImage*, *63*(1), 320–327. https://doi.org/10.1016/j.neuroimage.2012.06.062

Zhang, H., Chavarriaga, R., Gheorghe, L. A., & Millán, J. del R. (2013). Inferring Driver's Turning Direction through Detection of Error Related Brain Activity.

APPENDICES

Appendix I Informed Consent (Chinese Version)



香港理工大學康復治療科學系科研同意書

研究題目：
不同目標維持與快速適應的需求對由上而下雙網絡控制的認知任務表現的影響：經顱磁刺激與腦電波研究

研究人員：
林樂恆先生、陳子頌博士 、陳智軒教授

科研內容：
研究目的：在不同目標維持與快速適應的需求下，透過經顱磁刺激探討由上而下控制雙網絡對進行認知任務表現的不同影響。

研究程序：在第一天，你需要填寫個人資料問卷及接受認知功能的甄別試。然後你將會參與一項有關認知的實驗。在實驗進行期間，在你右邊顱骨的其中三個位置會接受穿顱磁刺激。在第二天，你你將會只需參與一項有關認知的實驗。在實驗進行期間，在你右邊顱骨的另外三個位置會接受穿顱磁刺激。整個實驗為期二天，第一天與第二天分別為約七小時與五小時。若在過程中感到疲倦，你可稍作休息。

對項目參加者的益處：在參與本研究項目的過程中，參與者會更加深入了解自己上對下控制功能。更多資料會再實驗後提供。

潛在危險性：經顱磁刺激不適用於頭部有植入金屬之人士。有部分人會在經顱磁刺激時或之後感到頭痛或頭暈。這些情況是短暫的，並會在數小時之內完全消失。現在進行的實驗，是參照過往研究所用之刺激方案，使用的刺激強度將會遠低於引起腦癇的安全範圍。如在經顱磁刺激期間引起任何不能忍受之不適，你可以通知實驗員立刻停止該次刺激。你亦有權在任何時間及任何程序下終止問卷調查而不會受到任何懲處。而所有收集的數據將絕對保密。

同意書：

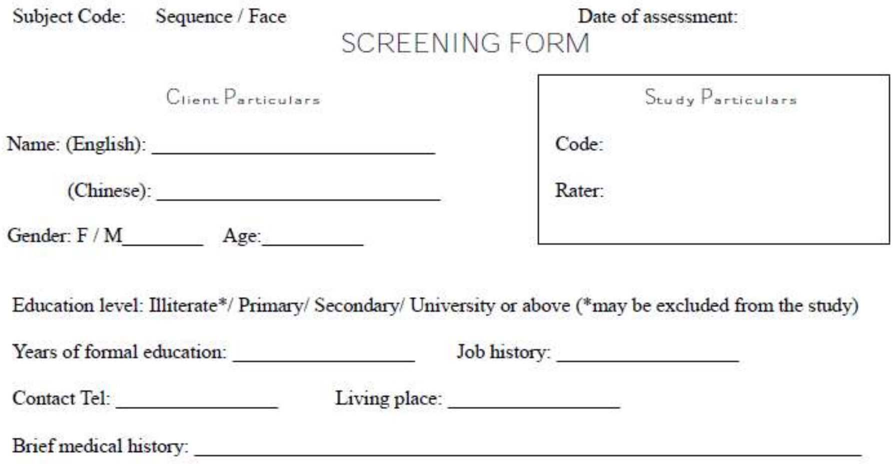
本人____________已瞭解此次研究的具體情況。本人願意參加此次研究，本人有權在任何時候、無任何原因放棄參與此次研究，而此舉不會導致我受到任何懲罰或不公平對待。本人明白參加此研究課題的潛在危險性以及本人的資料將不會洩露給與此研究無關的人員，我的名字或相片不會出現在任何出版物上。

本人可以用電話 2766 4310 來聯繫此次研究課題負責人，陳子頌博士。若本人對此研究人員有任何投訴，可以聯繫鍾小姐（部門科研委員會秘書），電話：2766 4329。本人亦明白，參與此研究課題需要本人簽署一份同意書。

簽名（參與者）：____________________ 日期：____________________

簽名（證人） ：____________________ 日期：____________________

Appendix II Demographic Data Form



Subject Code: Sequence / Face Date of assessment:

SCREENING FORM

Client Particulars

Name: (English): ____________________________

(Chinese): ____________________________

Gender: F / M________ Age:__________

Study Particulars

Code:

Rater:

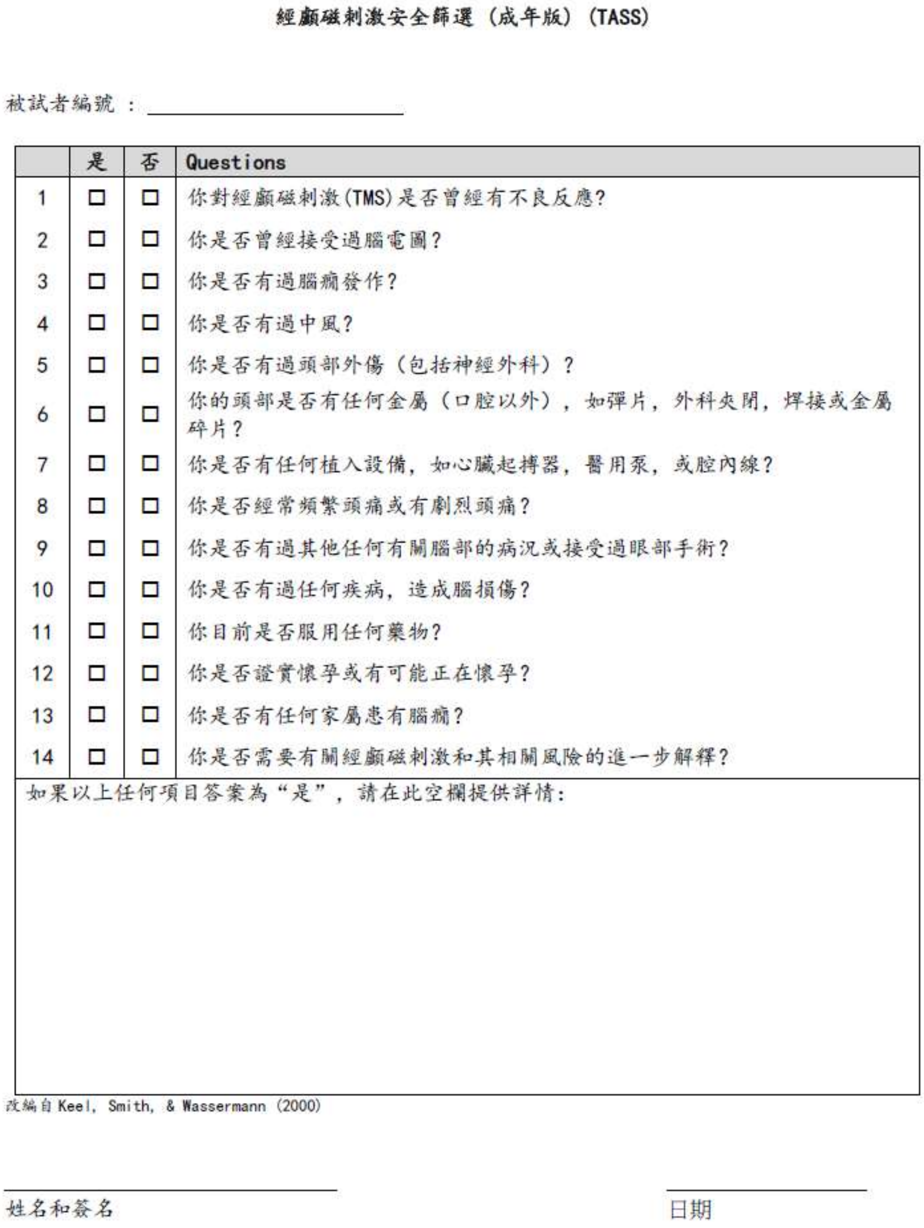
Education level: Illiterate*/ Primary/ Secondary/ University or above (*may be excluded from the study)

Years of formal education: __________________ Job history: __________________

Contact Tel: ________________ Living place: _________________

Brief medical history: ____

Appendix III TMS Screening Form (Chinese Version)



經顱磁刺激安全篩選（成年版）(TASS)

被試者編號：＿＿＿＿＿＿＿＿＿＿

	是	否	Questions
1	□	□	你對經顱磁刺激(TMS)是否曾經有不良反應?
2	□	□	你是否曾經接受過腦電圖？
3	□	□	你是否有過腦痫發作？
4	□	□	你是否有過中風？
5	□	□	你是否有過頭部外傷（包括神經外科）？
6	□	□	你的頭部是否有任何金屬（口腔以外），如彈片，外科夾閉，焊接或金屬碎片？
7	□	□	你是否有任何植入設備，如心臟起搏器，醫用泵，或腔內線？
8	□	□	你是否經常頻繁頭痛或有劇烈頭痛？
9	□	□	你是否有過其他任何有關腦部的病況或接受過眼部手術？
10	□	□	你是否有過任何疾病，造成腦損傷？
11	□	□	你目前是否服用任何藥物？
12	□	□	你是否證實懷孕或有可能正在懷孕？
13	□	□	你是否有任何家屬患有腦痫？
14	□	□	你是否需要有關經顱磁刺激和其相關風險的進一步解釋？

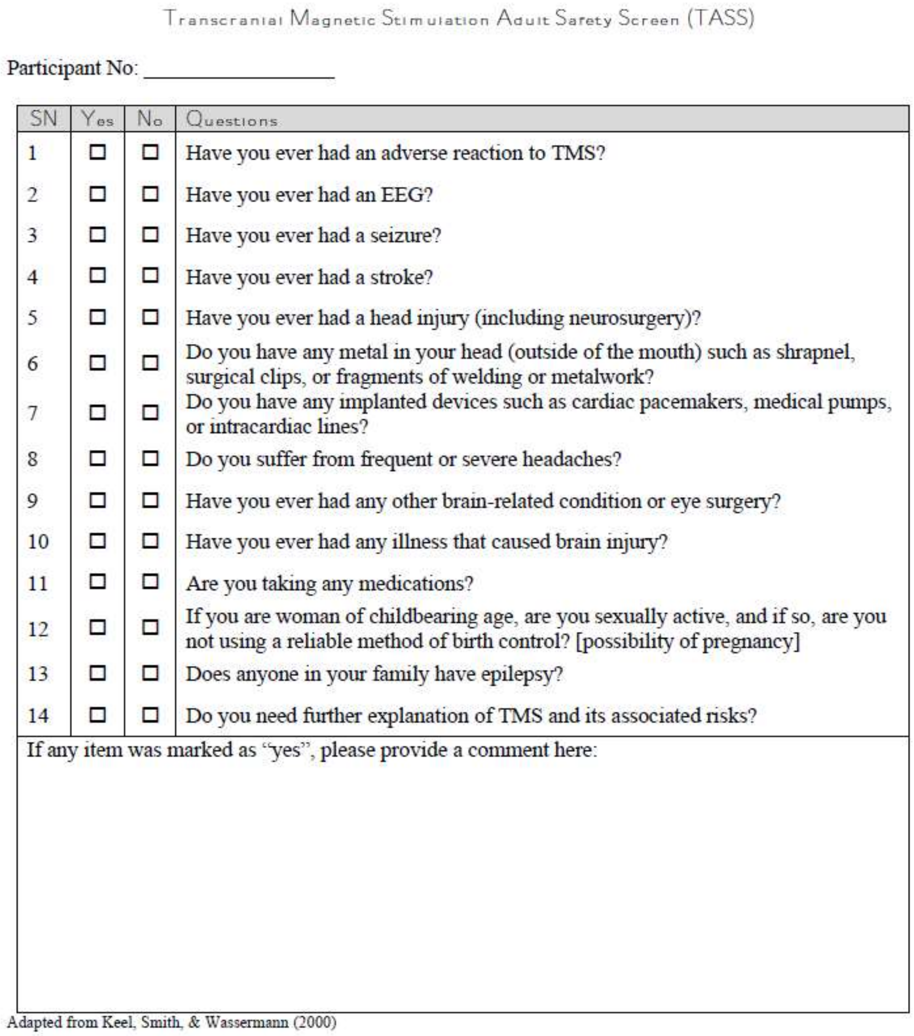
如果以上任何項目答案為“是”，請在此空欄提供詳情：

改編自 Keel, Smith, & Wassermann (2000)

＿＿＿＿＿＿＿＿＿＿＿＿　　　　＿＿＿＿＿＿＿＿

姓名和簽名　　　　日期

Appendix IV Screening Form (English Version)



Transcranial Magnetic Stimulation Adult Safety Screen (TASS)

Participant No: ________________

SN	Yes	No	Questions
1	☐	☐	Have you ever had an adverse reaction to TMS?
2	☐	☐	Have you ever had an EEG?
3	☐	☐	Have you ever had a seizure?
4	☐	☐	Have you ever had a stroke?
5	☐	☐	Have you ever had a head injury (including neurosurgery)?
6	☐	☐	Do you have any metal in your head (outside of the mouth) such as shrapnel, surgical clips, or fragments of welding or metalwork?
7	☐	☐	Do you have any implanted devices such as cardiac pacemakers, medical pumps, or intracardiac lines?
8	☐	☐	Do you suffer from frequent or severe headaches?
9	☐	☐	Have you ever had any other brain-related condition or eye surgery?
10	☐	☐	Have you ever had any illness that caused brain injury?
11	☐	☐	Are you taking any medications?
12	☐	☐	If you are woman of childbearing age, are you sexually active, and if so, are you not using a reliable method of birth control? [possibility of pregnancy]
13	☐	☐	Does anyone in your family have epilepsy?
14	☐	☐	Do you need further explanation of TMS and its associated risks?

If any item was marked as “yes”, please provide a comment here:

Adapted from Keel, Smith, & Wassermann (2000)

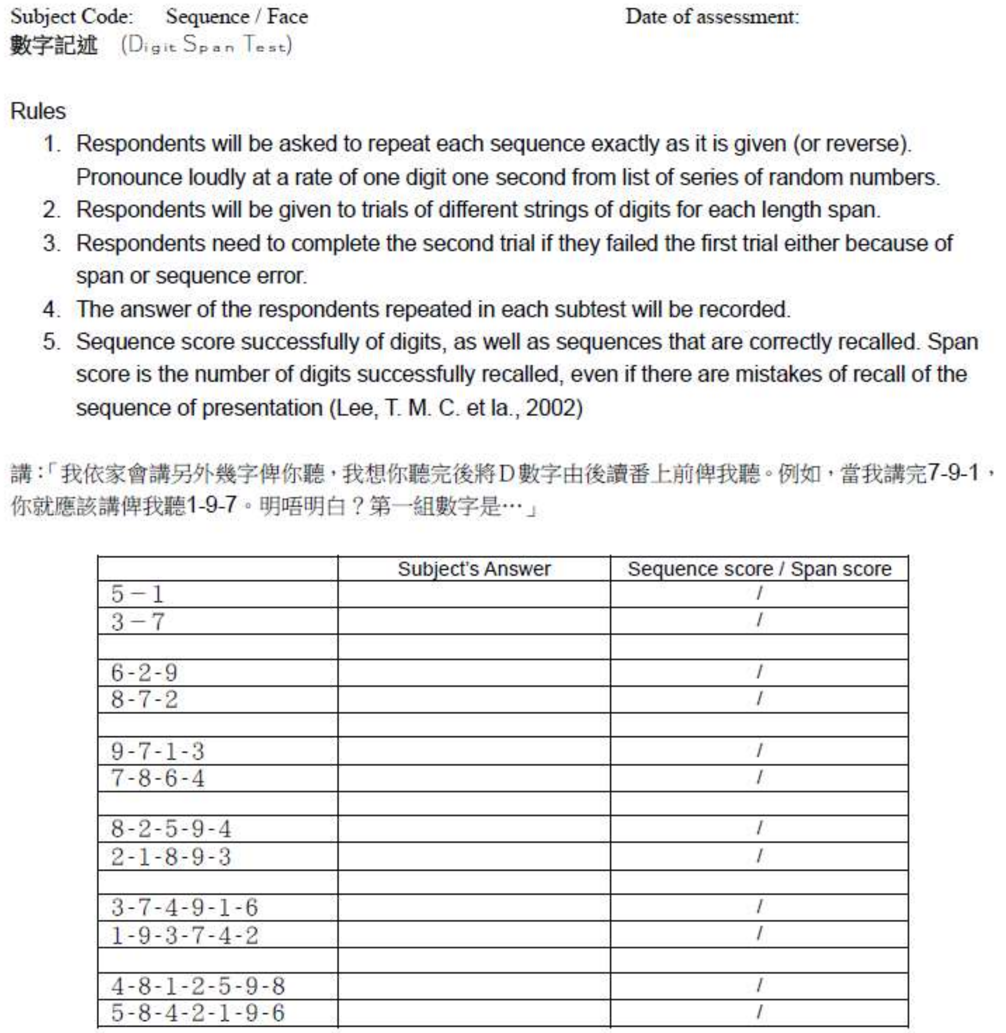
____

Name and Signature

____

Date

Appendix V Digit Span Test- Backward



Subject Code: Sequence / Face Date of assessment:

數字記述 (Digit Span Test)

Rules

1. Respondents will be asked to repeat each sequence exactly as it is given (or reverse). Pronounce loudly at a rate of one digit one second from list of series of random numbers.
2. Respondents will be given to trials of different strings of digits for each length span.
3. Respondents need to complete the second trial if they failed the first trial either because of span or sequence error.
4. The answer of the respondents repeated in each subtest will be recorded.
5. Sequence score successfully of digits, as well as sequences that are correctly recalled. Span score is the number of digits successfully recalled, even if there are mistakes of recall of the sequence of presentation (Lee, T. M. C. et la., 2002)

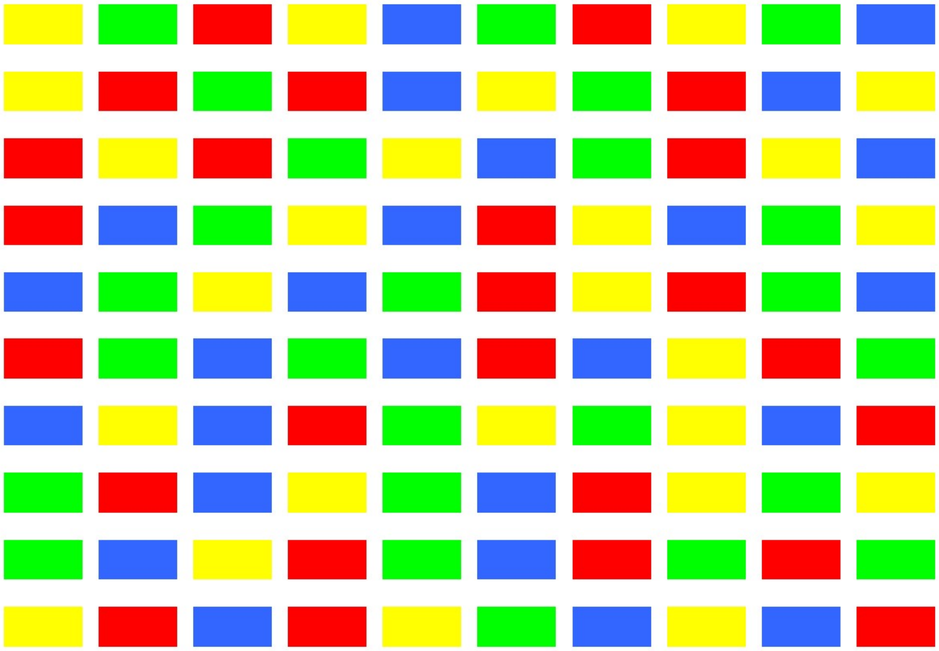
講：「我依家會講另外幾字俾你聽，我想你聽完後將D數字由後讀番上前俾我聽。例如，當我講完7-9-1，你就應該講俾我聽1-9-7。明唔明白？第一組數字是…」

	Subject's Answer	Sequence score / Span score
5 − 1		/
3 − 7		/
6-2-9		/
8-7-2		/
9-7-1-3		/
7-8-6-4		/
8-2-5-9-4		/
2-1-8-9-3		/
3-7-4-9-1-6		/
1-9-3-7-4-2		/
4-8-1-2-5-9-8		/
5-8-4-2-1-9-6		/

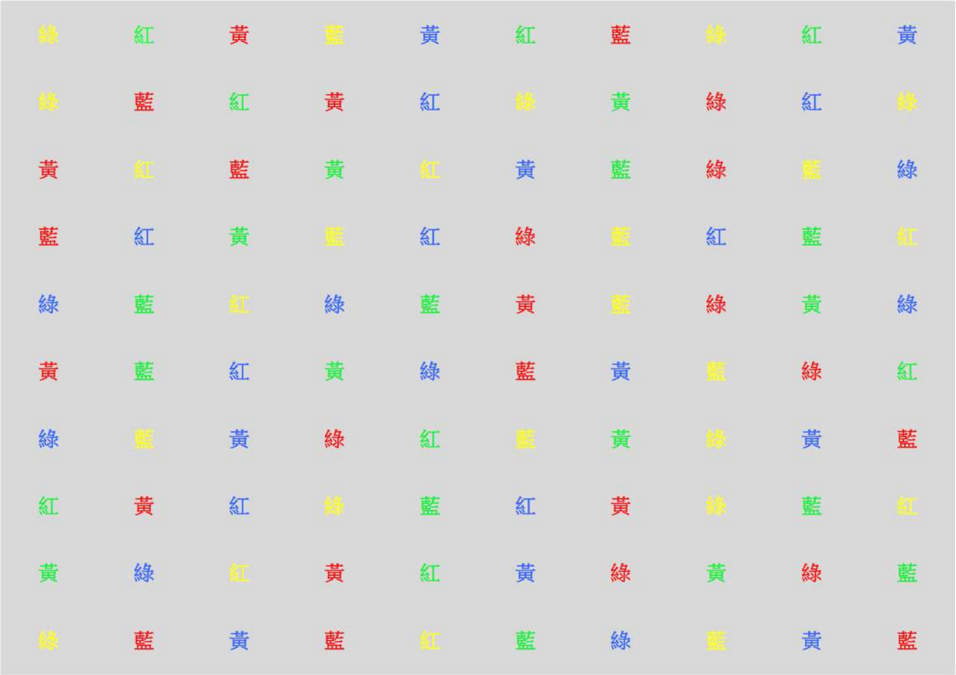
Appendix VI Stroop Test – Word Reading

綠	紅	黃	藍	黃	紅	藍	綠	紅	黃
綠	藍	紅	黃	紅	綠	黃	綠	紅	綠
黃	紅	藍	黃	紅	黃	藍	綠	藍	綠
藍	紅	黃	藍	紅	綠	藍	紅	藍	紅
綠	藍	紅	綠	藍	黃	藍	綠	黃	綠
黃	藍	紅	黃	綠	藍	黃	藍	綠	紅
綠	藍	黃	綠	紅	藍	黃	綠	黃	藍
紅	黃	紅	綠	藍	紅	黃	綠	藍	紅
黃	綠	紅	黃	紅	黃	綠	黃	綠	藍
綠	藍	黃	藍	紅	藍	綠	藍	黃	藍

Appendix VII Stroop Test – Color Naming

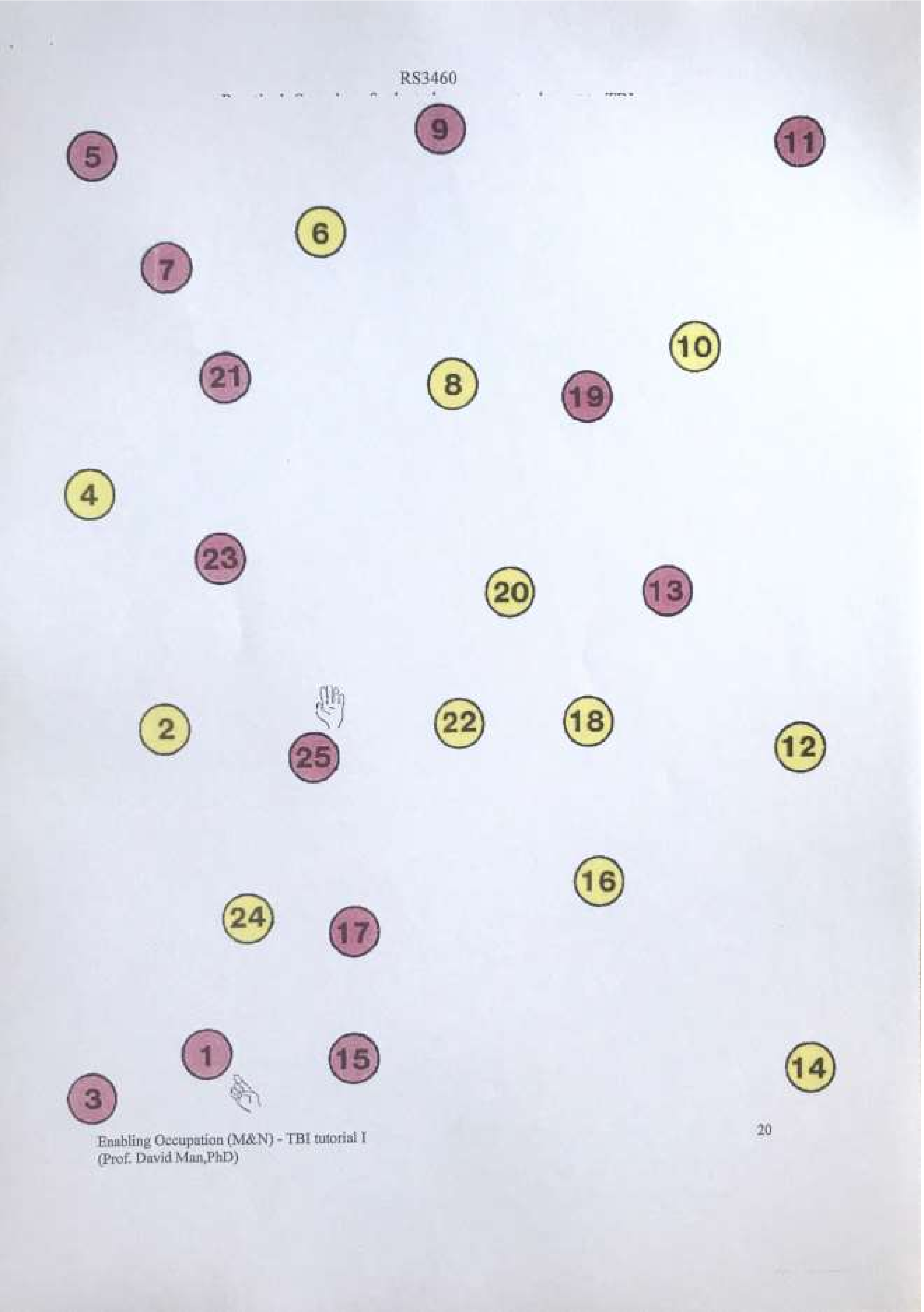


Appendix VIII Stroop Test – Incongruent Color Naming



綠	紅	黃	藍	黃	紅	藍	綠	紅	黃
綠	藍	紅	黃	紅	綠	黃	綠	紅	綠
黃	紅	藍	黃	紅	黃	藍	綠	藍	綠
藍	紅	黃	藍	紅	綠	藍	紅	藍	紅
綠	藍	紅	綠	藍	黃	藍	綠	黃	綠
黃	藍	紅	黃	綠	藍	黃	藍	綠	紅
綠	藍	黃	綠	紅	藍	黃	綠	黃	藍
紅	黃	紅	綠	藍	紅	黃	綠	藍	紅
黃	綠	紅	黃	紅	黃	綠	黃	綠	藍
綠	藍	黃	藍	紅	藍	綠	藍	黃	藍

Appendix VIIII Color Trails Test-I

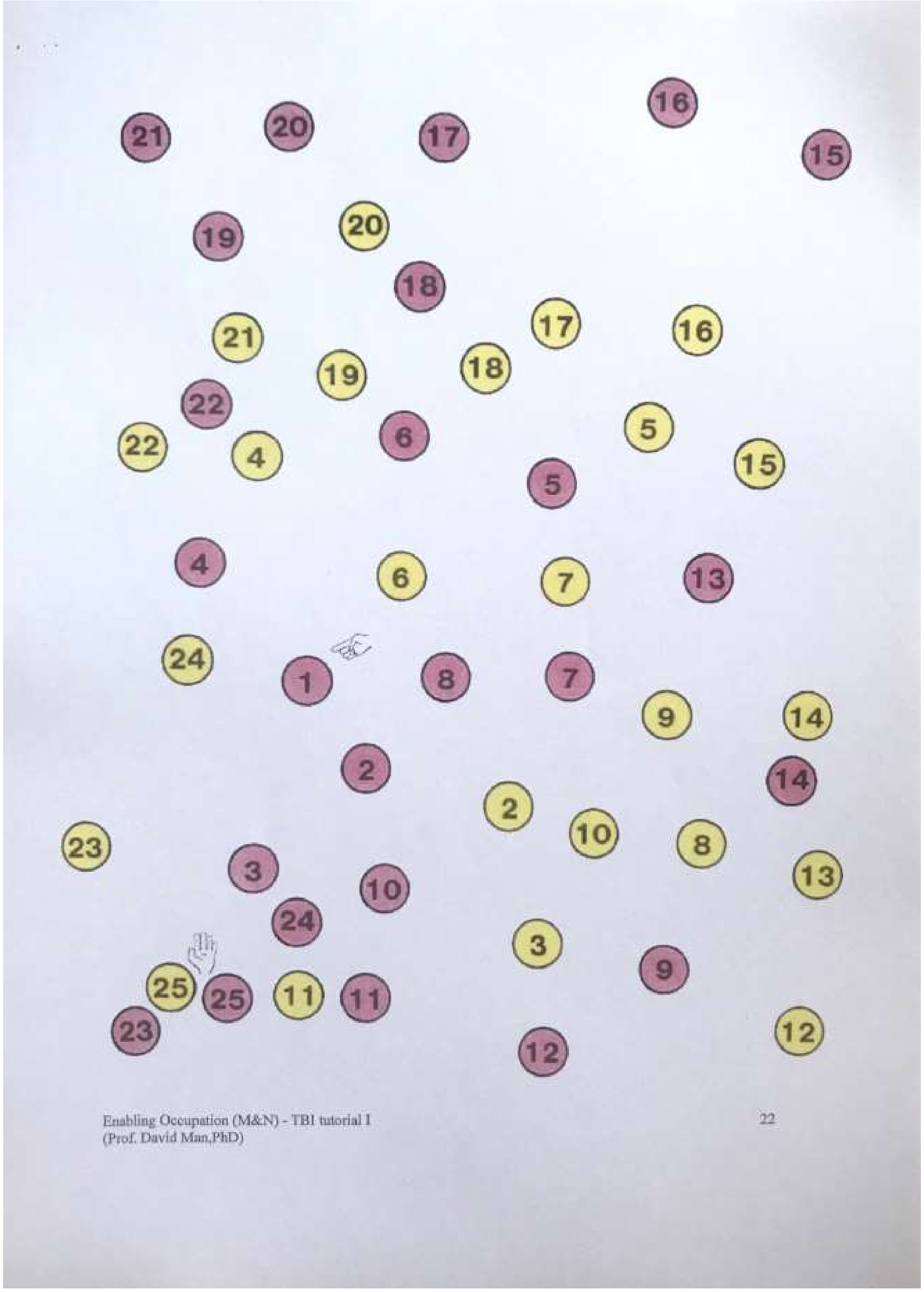


RS3460

Enabling Occupation (M&N) - TBI tutorial I
(Prof. David Man,PhD)

20

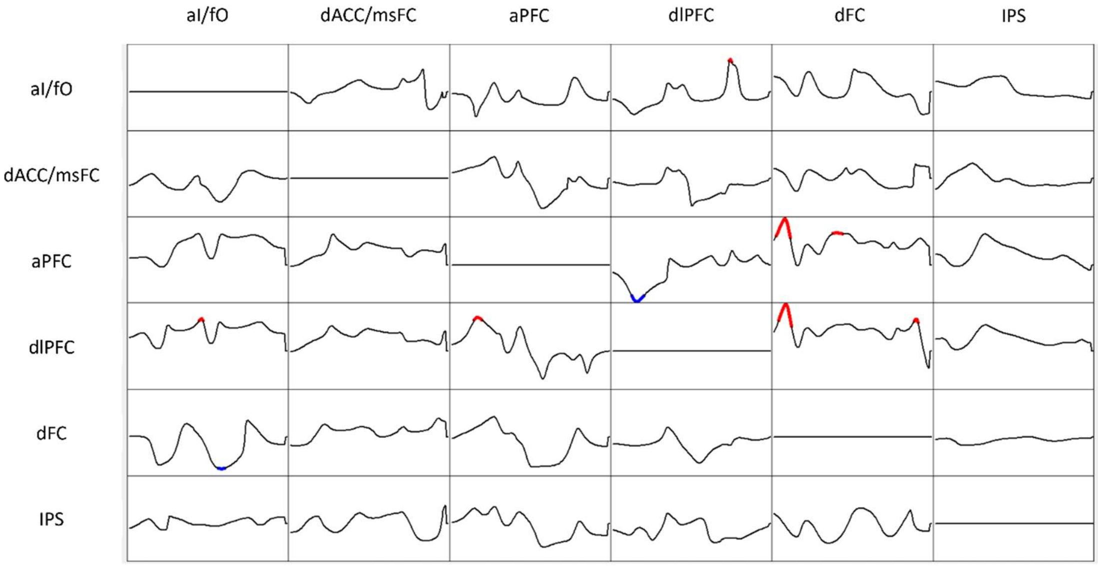
Appendix X Color Trails Test-II



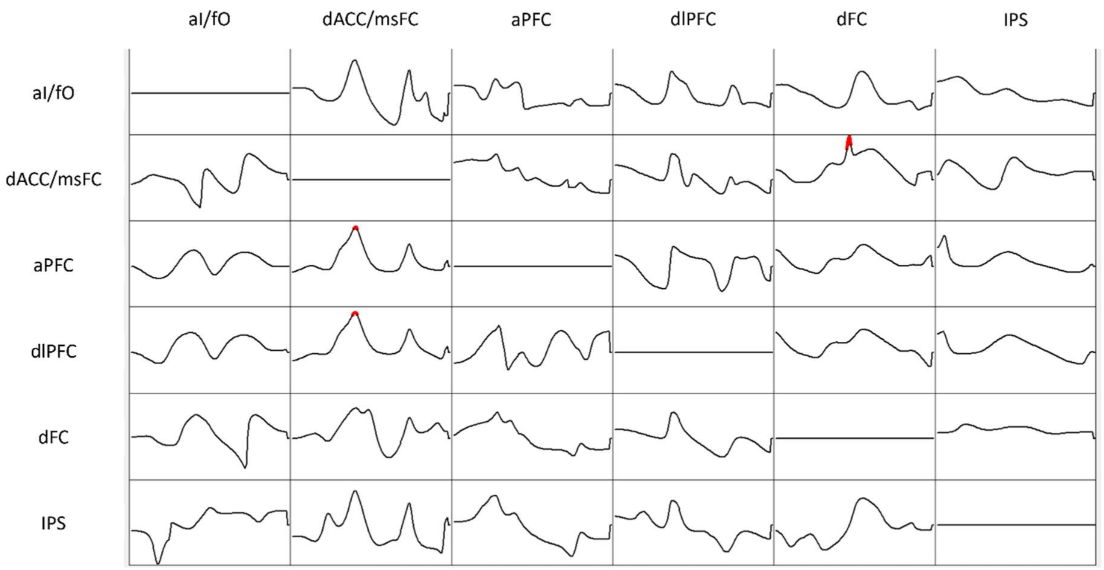
Enabling Occupation (M&N) - TBI tutorial I
(Prof. David Man,PhD)

22

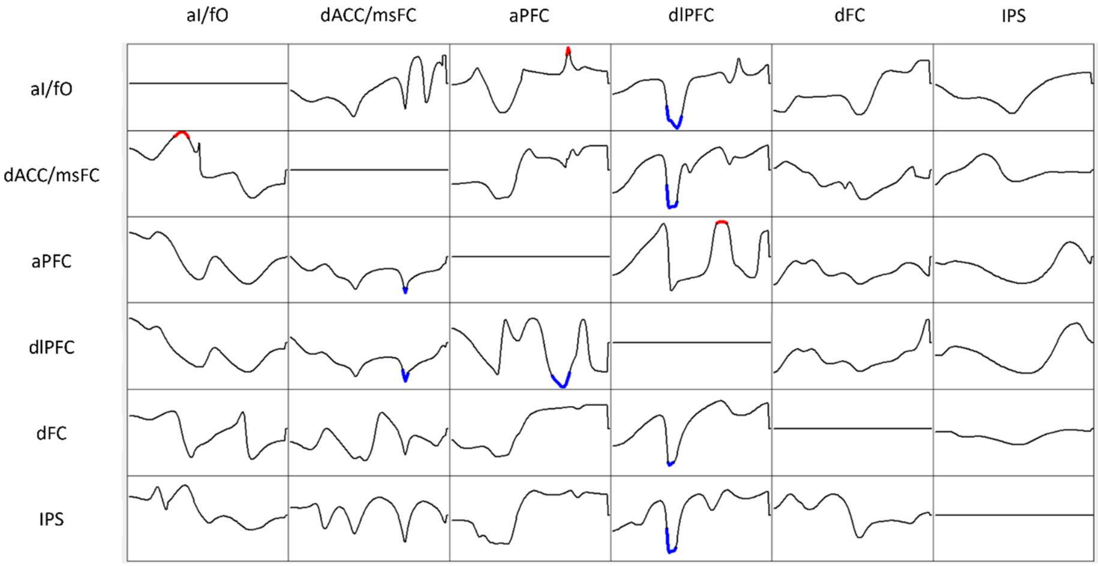
Appendix XI Output of ICoh Data of the Theta-banding Oscillation during Incongruent Trials of Dual-task Condition after Stimulating at aI/fO



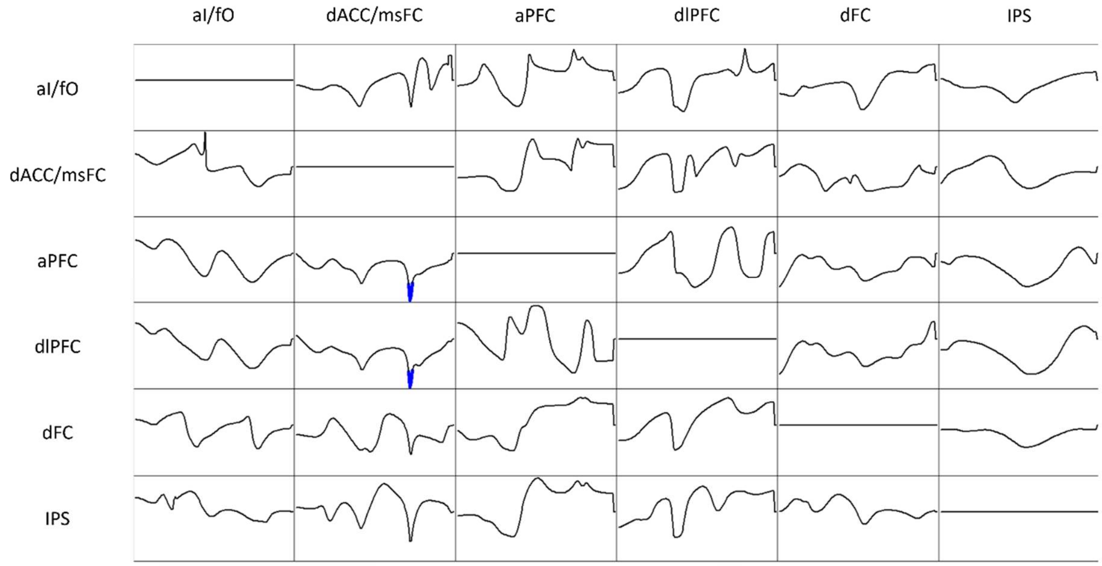
Appendix XII Output of ICoh Data of the Theta-banding Oscillation during Incongruent Trials of Single-task Condition after Stimulating at dlPFC



Appendix XIII Output of ICoh Data of the Alpha-banding Oscillation during congruent Trials of Dual-task Condition after Stimulating at aI/fO



Appendix XIII Output of ICoh Data of the Alpha-banding Oscillation during congruent Trials of Dual-task Condition after Stimulating at aPFC



Appendix XIII Output of ICoh Data of the Alpha-banding Oscillation during congruent Trials of Dual-task Condition after Stimulating dlPFC